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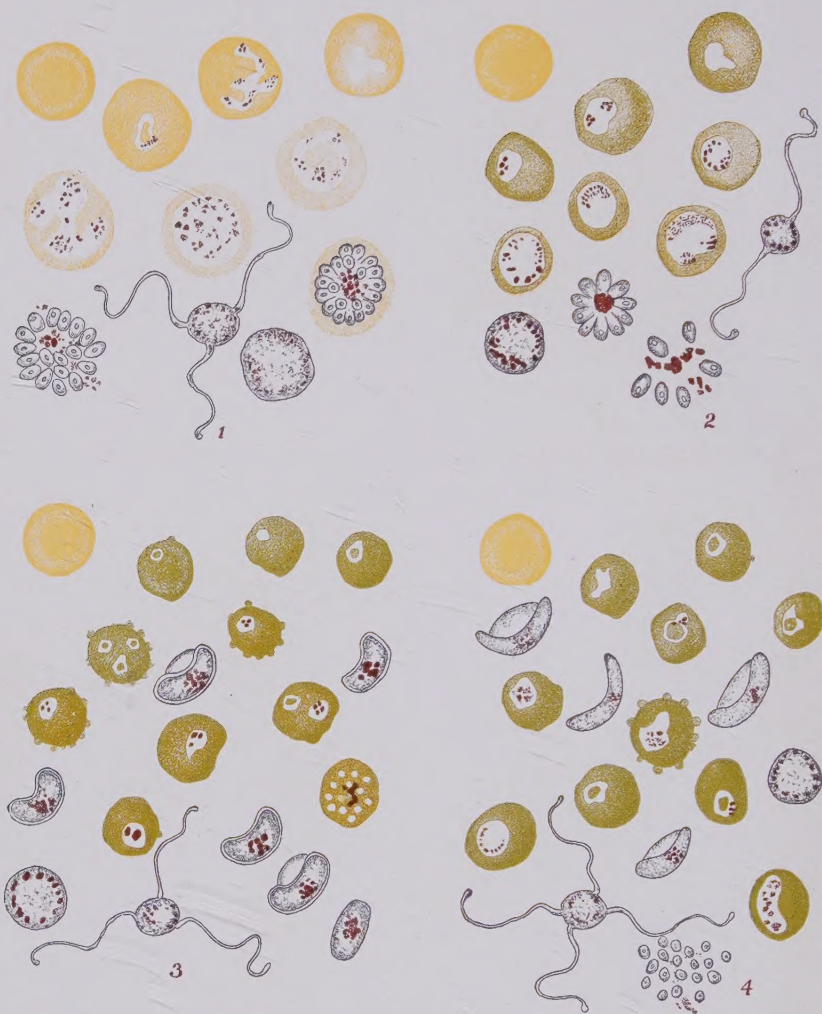


FIG. 1.—Illustrating the different forms of the malarial parasite.

1. The various stages in the life-cycle of the tertian parasite. (Note the large size and the pale color of the infected red blood-corpuscles and the light brown, fine, pigment granules.)

2. Various stages in the life-cycle of the quartan parasite. (Note the smaller size and darker color of the infected corpuscles and the larger, darker granules of pigment.)

3. Various stages in the life-cycle of the quotidian estivo-autumnal parasite. (Note the smaller size and the darker green color of the infected corpuscles, the minute size of the parasite, and the thick, plump crescents.)

4. Various stages in the life-cycle of the tertian estivo-autumnal parasite. (Note that the parasite is somewhat larger and the crescents longer and more narrow than the quotidian forms.)

INTERNATIONAL CLINICS

A QUARTERLY

OF

ILLUSTRATED CLINICAL LECTURES AND
ESPECIALLY PREPARED ORIGINAL ARTICLES

ON

TREATMENT, MEDICINE, SURGERY, NEUROLOGY, PEDIATRICS,
OBSTETRICS, GYNECOLOGY, ORTHOPEDICS,
PATHOLOGY, DERMATOLOGY, OPHTHALMOLOGY,
OTOLOGY, RHINOLOGY, LARYNGOLOGY,
HYGIENE, AND OTHER TOPICS OF INTEREST
TO STUDENTS AND PRACTITIONERS

BY LEADING MEMBERS OF THE MEDICAL PROFESSION
THROUGHOUT THE WORLD

EDITED BY

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VOLUME III. THIRTEENTH SERIES, 1903

PHILADELPHIA

J. B. LIPPINCOTT COMPANY

1903

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Diseases of the Gall-Bladder and Gall-Ducts

SOME MEDICAL ASPECTS OF THE DISEASES OF THE GALL-BLADDER AND GALL-DUCTS

AN ADDRESS DELIVERED AT THE SIXTH TRIENNIAL CONGRESS OF AMERICAN PHYSICIANS AND SURGEONS, HELD IN WASHINGTON, D. C., MAY, 1903

BY JOHN H. MUSSER, M.D.

Professor of Clinical Medicine, University of Pennsylvania; President-Elect of the American Medical Association

INTRODUCTION

IT seems almost a work of supererogation to discuss the subject that we are to consider to-day. In recent months so many and valuable have been the papers published that it has seemed as though the very words were taken out of the writer's mouth, so that what is to be said to-day smacks to him of repetition.

Comparison with Appendicitis.—It need not, however, be vain repetition. The era we are about to enter upon bodes for good. In the treatment of gall-bladder infections it looks as if we would go through the cycles of activity and inactivity, as in the early periods of our knowledge of appendicitis.

Primary Disease to be Treated.—We trust that this contribution will further the progress which the writer sincerely believes is the true one, to the end that primary disease of the gall-bladder and gall-ducts will be accurately diagnosed, and precisely and hence thoroughly treated, so that secondary disease will be relatively rare. Local causes, such as displacements and conditions which give rise to external pressure, must be removed. As forced upon us now, it is secondary manifestations that we have to contend against, manifestations which imply complications so difficult to manage as to render the mortality of alarming proportions.

Secondary Disease Fatal.—The opprobrium of the medical and surgical treatment of gall-duct and gall-bladder affections arises because the death-rate in secondary affections is so high. Let us see to it that the primary ailments are cared for, blocking thereby the oncoming of secondary conditions.

Prognosis.—If primary processes are recognized in the future, cholelithiasis with its enormous train of abnormal states, obstructions and dilatations, will be prevented. Modern treatment of these affections will result in success in the highest aim of our endeavor, prevention. Fifty years from now the many secondary phenomena will be as rare as those which are secondary to diseased conditions now removed early, such as cataract, appendicitis, vesical calculus, and a host of other conditions. Students of that period will marvel at the reports of the cases of the present.

Morbid Anatomy of the Future.—It is interesting to picture what a blank there may be in the morbid anatomy of biliary affections fifty years hence. The present day pathologist should make haste to fit out his anatomical museum to full completion in respect to biliary pathology. We can point out that notwithstanding the extraordinary multiplicity of primary and secondary lesions, our museums contain but few illustrations of these processes.

Museum Specimens Few.—A search of the museums of Philadelphia disclosed less than twenty prepared specimens, excluding gall-stones, which a student could consult.

Surgeon's Need.—This was not surprising, for the writer has seen surgeon after surgeon operate on biliary disease when they had no conception of the anatomical complications that arise, as in a case of prolonged cholecystitis and cholelithiasis, and they readily became involved, indeed lost, in a morbid anatomy quagmire as effectually as if thrown into a yawning abyss in the dismal swamp. The first precept the writer would urge is, Surgeons should know morbid anatomy.

Terminal Infections.—Before leaving the field of morbid anatomy, a word further. My own studies have impressed me with the great frequency with which disease of the gall-bladder and gall-ducts lead to the termination of life. In many, many cases, put down as senility, in cases of chronic disease, as tuberculosis, nephritis, cardiac disease, death has not been due to these affections, but to terminal infections, the source of which was in the biliary appa-

ratus. Terminal infections will therefore be prevented by the removal of primary foci of disease.

GENERAL SUMMARY

Morbid States.

A. The primary morbid states of the gall-bladder and gall-ducts are:

Inflammations { catarrhal (rare).
infectious.

Morbid growths (primary).

Parasitic invasions.

B. The secondary morbid states are:

(1) Causes outside of the gall-bladder and gall-ducts.

Inflammations { catarrhal { secondary to heart, lung,
infectious { or abdominal disease.

Morbid growths.

Obstructions { displacements and deformities.
diseases outside of the ducts.

(2) Causes within the gall-bladder and gall-ducts.

Inflammations (including ulceration and perforation).

Because of { displacements and deformities.
morbid growths.

Foreign bodies { parasites.
gall-stones.

Obstructions, because of

Inflammations,
Morbid growths,
Foreign bodies.

Enlargements, because of

Inflammations,
Morbid growths,
Foreign bodies,
Obstructions.

Unfortunately, the states which clinicians see are in the large proportion of cases secondary, and belong to

(1) Local disease, as indicated above.

(2) Diseases in remote parts.

PRIMARY MORBID STATES

INFLAMMATION OF THE GALL-DUCTS. CATARRHAL CHOLANGITIS

Causes.—The disease is secondary to gastroduodenal catarrh, to pressure, to local spreading infections. Other cases of catarrhal jaundice are found to be primarily infectious.

The *symptoms* and signs are well known. The age of the patient, the presence of a cause, and the clinical course make up the picture. When long continued, catarrhal inflammation may resemble obstruction due to other primary or secondary processes.

The *diagnosis* in cases of so-called catarrhal jaundice continuing more than six weeks should be revised if the erythrocytes fall in number, the hemoglobin drops, the spleen enlarges, and there is loss of weight. The true nature of the disease can be determined by the antecedents or by accompaniments, which by this time may be more prominent, such as the enlarged glands of syphilis or tuberculosis. Organic diseases, cirrhosis, cancer of the liver, infections, as Weil's disease, must be excluded. Many so-called catarrhs are the result of typhoid, pneumococcus, or other infections.

Treatment. — *Medicinal.* — Hydrotherapy, including an abundance of water internally; enemas of cold water (Krull); compresses; baths. Proper diet (Carlsbad at home). Clothing. Exercise. Rest. Alkalies; iron, if anemic. Ammonium chlorid.

Surgical.—Symptomatic operative interference is compulsory, if the obstruction is complete, jaundice prolonged, the patient toxic, and the liver or the spleen enlarged.

SUPPURATIVE CHOLANGITIS

Suppurative cholangitis simulates pyelophlebitis, abscess of the liver, syphilis of the liver, rare cases of cancer, and Weil's disease.

Diagnosis is based on: (1) *Clinical Course.* — The onset is gradual. There is infection of the ducts or the gall-bladder; foreign bodies, as gall-stones, are present, or there was a previous general infection.

(2) *Objective Diagnosis.*—Icterus may or may not be present. The fever is characteristic (hectic type). Toxic symptoms from sepsis of jaundice occur.

(3) *Physical Diagnosis.*—The liver is enlarged moderately and tender. There is a tender area in the region of the twelfth dorsal vertebra, from 2 to 3 cm. from the middle line (Boas).

(4) *Laboratory Diagnosis*.—Leukocytosis. Serum reaction to determine cause. Blood examination to exclude malaria.

Differential Diagnosis (see Infections).—Pyelophlebitis: absence of cause for infection in the portal area. Amebic abscess: clinical antecedents, physical diagnosis, and absence of leukocytosis. Malaria: blood examinations. Simple cholelithiasis: no leukocytosis (see Ball-valve Calculus).

Treatment consists of drainage. Patience and waiting are of doubtful value.

CHOLECYSTITIS

Cholecystitis simulates hyperemia and infections of the liver, sub-diaphragmatic abscess (see Mason's and Osler's papers), diaphragmatic pleurisy, pneumonia, pancreatic affections, perforations of ulcer of the stomach or duodenum, intestinal obstructions, uremia, and endocarditis.

Diagnosis is based on: (1) *Clinical Course*.—Primary cholecystitis follows acute gastroduodenitis, and general infections. Secondary cholecystitis follows infections induced by foreign bodies and obstruction. It occurs at any age and in either sex; habits of but little consequence. Antecedents mentioned above. The onset varies; is often fulminating, but may be mild and gradual or severe (see report of cases, pages 22 to 29).

(2) *Subjective Diagnosis*.—Pain from spasm or tension, tenderness, nausea, and vomiting.

(3) *Objective Diagnosis*.—Fever, mild to severe. Remittent or intermittent. Chills in fulminating type. Jaundice not present.

(4) *Physical Diagnosis*.—A tumor at the end of the ninth rib. Has the characteristics of a swollen gall-bladder; movable with respiration unless inhibited by pain. Spasm of rectus muscle.

(5) *Laboratory Diagnosis*.—Leukocytosis in all infections except those due to typhoid fever. Present in 50 per cent. of the latter. Serum diagnosis is important to determine the nature of the infection.

CHOLECYSTITIS IN TYPHOID FEVER

A local infection of the gall-bladder in typhoid fever may develop in the course of the disease—during the third or fourth week, or in the period of convalescence. All grades are seen. It may or may not be accompanied by cholangitis. If it occurs in

the course of the disease its onset may be marked by an increase in the temperature, varying with the intensity of the local infection. In mild forms the fever may become a little higher than the continued range that has preceded. In severe forms it may become remittent or intermittent, and chills are not uncommon.

Nausea and vomiting are common in the beginning and may continue for several days. Pain in the region of the gall-bladder, localized tenderness, and rigidity of the right rectus muscle develop with the fever.

Fulminating cases, simulating perforation of the bowel, may occur during the course of the disease.

The mode of onset and association with cholangitis is illustrated by Case II. The symptoms are very characteristic. Pain is often so extreme as to simulate gall-stones or lead to collapse. It is usually in the situation described, but may be referred to the epigastrium. The pain may seem to be general at first and even be marked away from the gall-bladder, as in the right iliac fossa. Often the pain is diffused during the first 24 hours and attended by general rigidity and distention. Frequently the local symptoms are overlooked, and I am convinced that many cases of so-called relapse in typhoid fever are due to mild cholecystitis.

Leukocytosis need not be present. The data is quite insufficient concerning this point. In one of my cases it was absent, although following the law of leukocyte increase, such absence might have been due to the extreme infection.

Cholecystitis during convalescence from typhoid fever is not unusual. Contrary to Da Costa's experience, I have seen it quite as frequently at this period as at any other. Here, too, the cases may be mild, fulminating, and perforating. Case III will illustrate the onset and course of a fulminating attack.

Briefly, the case (III) seen with Dr. Rehfuess was one of typhoid fever of long duration in a woman, 56 years of age. Five days after the temperature was normal she was seized suddenly with severe diffuse abdominal pain. The greatest tenderness seemed to be confined to the right iliac fossa. She had a chill coincidentally, followed by fever and much prostration. I saw her two days after the onset of pain. Although no defined tumor was present the pain, rigidity, and tenderness were confined to the right upper quadrant; vomiting persisted, tympany was marked. Three hours after my

visit Dr. Edward Martin operated. In the interval the signs of inflammation extended over the upper abdomen. The gall-bladder was much enlarged and attached to neighboring organs by adhesions. It contained mucus and pus, both bile stained. There were no calculi, and the ducts seemed free. Operation was followed by immediate relief and an uninterrupted convalescence (see charts).

Case IV was one of onset more gradual after the typhoid process was completed. It is interesting to note that tenderness was absent, leukocytosis was absent, while chills and fever were dominant features. The chart herewith exhibited shows the course of the fever. The occurrence of death from acute hemorrhagic pancreatitis is most interesting in the light of recent researches.¹

The onset in the post-febrile period takes place in the first or second week, when we are about to place the patient on solid food. In consequence, the change of diet is held responsible for the pain, tympany, and fever.

DIFFICULTY IN RECOGNIZING SECONDARY CHOLECYSTITIS

Cholecystitis occurring in a subject who has gall-stones or a displaced liver differs from primary cholecystitis in local rather than general symptoms. The altered position of the gall-bladder changes the location of the pain and tumor. In a case operated on by Dr. Harte the tumor was below the transverse umbilical line, and in one operated on by Dr. Price the tumor was in the median line and the gall-bladder had emptied its contents into the lesser peritoneal cavity. In the first case the tumor was continuous with the liver dulness, in the second it was not. It is scarcely necessary to say that the antecedent history of cholelithiasis aided in the diagnosis.

DIFFERENTIAL DIAGNOSIS

My experiences of the past year have led me to believe that cholecystitis can easily be recognized, the difficulty arising in distinguishing some forms of it from appendicitis being greatest, and yet these are cases of secondary cholecystitis and therefore more obscure because due to displaced gall-bladders. Primary cholecystitis can be recognized by the clinical course, the physical signs, and

¹ Since this paper was read, Moynihan has reported a similar case in the Brit. Med. Jour., 1903, i, 1350. These are the first cases of this character reported.

the associate symptoms, together with the results of laboratory diagnosis.

In the distinction between the *cátarrhal* and *suppurative* varieties we are deciding in part between mild and severe forms of infection. The degree of the infection is estimated by the severity of the local symptoms and the intensity of the toxemia as indicated by the fever, the cardiovascular and cerebral symptoms, and the leukocytosis. It is to be remembered that an intense alarming inflammation may arise without pus formation, as in Case I. A clear fluid was removed from the gall-bladder.

The following diseases are to be considered in the differential diagnosis:

(1) *Congestion of the Liver*.—In cases of acute infectious endocarditis with cardiac dilatation, the left lobe of the liver often enlarges and is the seat of pain and great tenderness. This is accompanied by jaundice. An enlarged gall-bladder may be simulated, and as the general symptoms of infection prevail, that organ may be considered the site of primary infection. It is not unusual to have endocarditis without physical signs in the heart. Again, in a case of purulent pericarditis under my care, the distention of the liver capsule was extreme, pain was excessive, and the picture was not unlike that of suppuration of the biliary passages.

(2) *Syphilis of the Liver*.—The history may help, but who does not know how weak such help is in this infection. Antecedent and associate conditions aid us here. The fever is commonly intermittent in syphilis. The paroxysms are at fixed periods in the day, however. Leukocytosis is absent. Justus's sign is not satisfactory. A localized tumor with the characteristics of an enlarged gall-bladder is usually not present. It may, however, exist, although it is not so tender. A female patient of mine, aged 32 years, who had been exposed to the possibility of infection, was seized with pain, tenderness, and swelling in the gall-bladder region. She was told it was "cold" or "gall-stones." Jaundice followed. The local tenderness and tumor continued but the jaundice disappeared. The mass simulated cancer of the pylorus. A moderate fever prevailed. Specific treatment dissipated the tumor, and all the symptoms vanished with it. There has been no recurrence in twelve years. A rapidly growing localized gumma attended by fever and sweats may simulate gall-bladder infection. It has been my experience to find a lymphocytosis more common in syphilis than in other infections.

(3) *Multiple Abscess of the Liver or Pyelophlebitis.—Portal Pyemia.*—The differential diagnosis is sometimes difficult or impossible. The antecedent history of abdominal infection is necessary to establish the diagnosis. The liver is large in multiple abscess; in cholecystitis the gall-bladder is large. Pain is not marked in multiple abscess. Ascites, enlarged spleen, hematemesis, and diarrhea are more common in portal obstruction.

(4) *Abscess of the liver* occurring in amebic dysentery is recognized by the history, by physical signs posteriorly rather than anteriorly, and often thoracic rather than abdominal, by the frequent absence of leukocytosis, the rarity of fever whose type is more or less slow, and by the presence of uniform enlargement or enlargement in one direction of the liver. The spleen is more likely to be enlarged in abscess than in non-typhoid cholecystitis. Abscess of the liver is neither as painful nor as acute an infection, and hence not as intense an infection as cholecystitis.

(5) *Secondary Cholecystitis.*—It is to be remembered that we are considering only the differentiation of primary cholecystitis and hepatic affections. Secondary cholecystitis and cholangitis have the history of the primary cause.

(6) *Subdiaphragmatic Abscess.*—History, physical signs, and exploratory puncture avail (see papers of Mason, Osler, and others). It manifests itself posteriorly, and signs are abdominal as well as thoracic. Difficulty of diagnosis is not great in primary cholecystitis.

(7) *Diaphragmatic Pleurisy.*—Diagnosis at times is difficult. Exposure to cold is a feature in pleurisy. The following incidents in a case under my care illustrated certain points in diagnosis: The patient, who was robust, although rheumatic, was operated upon for hemorrhoids. Three days later, after taking a cold bath, symptoms of diaphragmatic pleurisy, but suggestive of gall-bladder infection, developed. There were chill and fever, and rheumatism in other muscles, but there was no leukocytosis. The diagnosis of pleurisy was made.

(8) *Pneumonia.*—It is only necessary to call attention to the likelihood of confusing the infections in some cases. In pneumococcus infection with gastric and abdominal symptoms dominant, the pulse-respiration ratio and the expiratory grunt alone may suggest the lesion, especially in children. In those in whom jaundice occurs early the confusion may be increased.

(9) *Pancreatic Diseases*.—These have been so exhaustively considered at yesterday's session of this Congress that it is not necessary to take them up on this occasion.

(10) *Perforation of Gastric and Duodenal Ulcer*.—The diagnosis is sometimes difficult, but the marked difference in the previous history is most helpful. Without such carefully worked out history diagnosis may be impossible.

(11) *Intestinal Obstruction*.—This condition does not simulate hepatic and biliary disorders as frequently as it does pancreatic lesions. Time forbids an extensive review.

(12) *Uremia*.—Like hysteria, uremia can simulate almost any other condition. In that form in which abdominal pain and vomiting are most prominent, the surgeon may easily be led astray, particularly as albumin and casts are almost always present in gall-bladder infections.

PRIMARY CANCER OF THE GALL-BLADDER AND GALL-DUCTS

The literature of this affection has been thoroughly studied. The cases collected by the writer, Courvoisier, Sugist, Ames, Kely-nack, Rolleston, and others are accessible. It may be said that our knowledge of this condition is fairly definite.

PARASITES

Parasitic invasions of the biliary passages, as by hydatids or round worms, lead to obstruction of the ducts and perhaps enlargement of the gall-bladder, with secondary catarrhal or suppurative cholangitis. A shrewd guess at the diagnosis may be made by exclusion and by the antecedent history of these affections. Otherwise the cases fall under the head of inflammation or of obstruction of the biliary passages.

SECONDARY MORBID STATES

It is not within the province of this paper to consider all the lesions that arise secondarily to primary morbid states. A few will be considered. Thus it is important to consider *displacements* and *deformities* of the liver, as they give rise to many pathological conditions of the ducts or simulate gall-bladder diseases. It is hoped that this study of gross conditions will lead to the study of

less evident states, for the writer fully believes that displacements are leading etiological factors in biliary affections, and that we are ignorant of the relatively normal position of the liver and do not know when the liver is displaced in minor degrees. The prevention and treatment of minor displacements is obvious.

Morphology.—In regard to gall-stones and displacements it is rare to see cholelithiasis, not of infectious origin, in persons who are morphologically of normal type. The patient is too fat or too lean; too small in girth or perhaps too large; presents one of many abnormal types of thorax and abdomen.

DISPLACEMENTS AND DEFORMITIES¹

A. DISPLACEMENTS.—About 80 cases have been reported. Gall-bladder and gall-duct disease is simulated because

- (1) Gall-stone colic is simulated by obstruction of the ducts;
- (2) Of obstructive jaundice due to kinking of the ducts;
- (3) The tumor simulates a gall-bladder tumor.

Diagnosis.—General morphology is suggestive. Clinical course. Females. History of trauma or abdominal disease. Diastasis. Long duration. Recurrent attacks of pain, transient jaundice, bilious vomiting. Symptoms of pressure upon other organs. Neurasthenia. Gastro-enteroptosis. Fever absent, except in a few cases.

Physical Examination.—(1) Tumor of the size, shape, consistence, and movability of the liver.

- (2) Tympanitic note over the normal area of liver dulness.

Note.—Percuss in the upright and the recumbent postures.

Exception.—Anteversion of liver when convex surface is in contact with the diaphragm and the anterior abdominal walls—dulness not absent.

- (3) Palpation by Glenard's procédé du pouce.
- (4) Replaced by palpation or recumbent posture.

¹ Literature:

Landau, *Die Wanderleber*, etc., 1885.

Faure, *Thèse de Paris*, 1892.

Graham, *Trans. Assoc. Amer. Phys.*, 1895, x, 258. (Résumé of 69 cases.)

Packard, *Univ. Med. Mag.*, 1897.

Teleky, *Centralblatt für die Grenzgebiete der Medicin und Chirurgie*, 1901, p. 267.

Steele, *Experimental Evidences of Biliary Obstruction in Floating Liver*, *Univ. Med. Mag.*, Dec., 1902.

B. DEFORMITIES.—(1) *Floating Lobes*.—Riedel's lobe. Tongue-like process. Gall-bladder tumors simulated by elongated lobe.

Diagnosis.—Clinical course uneventful; or tumor in which attacks of pain and tenderness. Usual occurrence in women; history of abdominal constriction. Attacks of gall-stone colic and cholangitis, a coincidence or rarely a sequence.

Physical Examination.—Tumor movable with respiration, variable size, tongue-like, connection with liver may or may not be demonstrated by percussion. Palpation: movable, sometimes disappears. In rare instances behaves like floating kidney. Percussion: Dull if thick; resonant if thin. Solid, smooth.

Cholecystitis simulated by tumor, which at times is the seat of pain and tenderness. Cholelithiasis is a frequent accompaniment, and may give rise to confusion.

(2) *Corset Liver*.—Gall-bladder tumor simulated by this deformity.

Clinical Course.—Like that of floating lobe; often associated with incidents of hepatic disease, hence may be coincident with cholecystitis, cholangitis, cholelithiasis, gastro-enteroptosis, and carcinoma.

Physical Examination.—Tumor as in floating lobe. If separated from liver, variable in size and shape; consistence of liver; movable to an extreme degree; never in the loin; tender and swollen; always superficial; sometimes the seat of spontaneous pain.

LIMITATION OF OUR KNOWLEDGE IN BILIARY AFFECTIONS

We have much to learn of the pathology and clinical course of these affections.

(1) *Leukocytosis*.—We cannot as yet consider it more than a symptom. The recorded cases are few that give information either by numerical or differential count. My observations go to show that leukocytosis is present in all primary infections except typhoid fever; absent or uncertain in all secondary infections. Its presence therefore points to a primary lesion.

(2) *Hepatic Function*.—We have no clinical method of determining the degree or character of alteration of function in hepatic, much less biliary, disorders. The studies of Edsall, incorporated later, show how little we can rely on the urine for the clinical diag-

nosis of hepatic disorders. Perhaps we need a research hospital for the study of hepatic disease more than of any other organs.

(3) *Displacements* are obscure. We do not know what constitutes a displacement sufficient to predispose if not excite biliary disorder. The questions of morphology and preventive measures are too vast for discussion. It is not dislocations but minor displacements of which we must learn more. What degree of displacement gives rise to impeded circulation of the bile in the channels—interferes with bile drainage?

(4) *Treatment*.—We have now accurate knowledge of the effects of treatment. Do “cures” postpone the evil day? How many persons get well permanently and without secondary states always pending, if not in full blast? Is it worth while waiting for medicinal treatment in primary cases? How many get well in this manner and how many experience temporary cure, even if they get relief? Finally, do surgical measures in acute primary infections prevent secondary states? It seems too soon to answer the latter question. My personal experience supports the knife as the best cure in cholecystitis.

(5) *Morbid Anatomy*.—The young surgeon should see the autopsies of at least 500 cases of old people whereby at least 100 cases of secondary diseases of the gall-bladder and gall-ducts would be studied.

(6) *Operative Measures*.—When should an operation be advised? In catarrhal cholangitis, if chronic, that is, of six weeks' to two months' duration, with no improvement; if the blood is falling, if the time required for blood-clotting increases, and if the spleen and liver are enlarging, operation should be done. In *suppuration* operate in all cases, if no relief to any one symptom in three days; if the liver does not increase, if the fever falls, if the leukocytes fall, if jaundice improves, use expectant treatment. In *cholecystitis* operation perhaps should be performed in every case. Certainly operate in fulminating cases with sepsis and progressive toxemia; leukocytes increasing or stationary. If cultures or serum reaction indicate the infective organism, be guided by its character. A colon infection means operation. The question of operative interference must be decided not alone by laboratory investigation but by clinical sense. If a patient is sick to-day, sicker the next day, and is a little more toxic and septic each day, an operation should be done, in

spite of the absence of leukocytosis. The matter is one of degree of illness, and in each case the clinical acumen of the physician must stand in some service.

Nephritis is not a contraindication to operation. "Bile" and septic nephritis are quickly relieved by the operation.

DEFINITE KNOWLEDGE CONCERNING BILIARY AFFECTIONS

We deem that it can be said that we have fairly definite knowledge concerning diseases of the gall-bladder and gall-ducts. With the limitations already described borne in mind we can say we have a good clinical picture of

- (1) Acute catarrhal and suppurative cholangitis.
- (2) Cholecystitis.
- (3) Primary carcinoma.
- (4) Displaced or deformed liver if in excess.
- (5) Ball-valve calculus, a symptom group well worked out by Naunyn, Fenger, Osler, and others.
- (6) Courvoisier's law.
- (7) Points in physical diagnosis described under special diagnosis.
- (8) Points in laboratory diagnosis.

SPECIAL DIAGNOSIS OF AFFECTIONS OF THE BILIARY PASSAGES

We must determine if there is present,

A. As primary states,

Inflammation.

Morbid growth.

Parasitic invasion.

B. As secondary states,

Inflammation and its results.

Cholelithiasis.

Obstruction	{	displacements and deformity.
		inflammation.
		foreign bodies.
		external disease.

Morbid growth.

Enlargements.

The recognition of primary or secondary states can only be ob-

tained by the employment of all means of diagnosis at our command.

It may be said that *laboratory* and *physical diagnosis* are of the greater value in *primary* states of the biliary passages; *historical diagnosis* in the *secondary* states. Some points elicited by each method are herein detailed.

Subjective Diagnosis.—The various subjective symptoms and their vagaries are familiar. It is well to recall that the pain of gall-bladder disease is due to inflammation, to distention, to colic or spasm induced by a foreign body (gall-stones). The pain due to inflammation and spasm and simulating hepatic colic must be distinguished from:

(1) Diet's crises, in floating kidneys, which may be accompanied by jaundice.

(2) Crises occurring in dilated and displaced stomachs, first described by Kussmaul, due to kinking and stenosis of the first and second portions of the duodenum, especially if adhesions have taken place.

(3) Crises due to downward displacement of the liver (36 per cent. of cases—Steele).

(4) Renal calculi.

(5) Pancreatic pain.

Hemorrhagic pancreatitis.

Acute pancreatitis, occasional jaundice.

Pancreatic colic, crisis, and sometimes jaundice.

(6) Gastric ulcer with local peritonitis.

(7) Duodenal ulcer—jaundice in a small proportion of cases.

(8) Gastric neuroses.

(9) Abdominal pain of thoracic disease, as pneumonia, diaphragmatic pleurisy.

(10) Disease of the vertebræ—tuberculous and rhizomelic.

(11) Appendicitis.

(12) Intestinal pain.

Acute ileocolitis.

Lead colic.

Epigastric hernia.

(13) Gastric crises of locomotor ataxia.

(14) Peritoneal pains of toxic origin often occurring in uræmia—pain in upper half of abdomen, more or less collapse with nausea and vomiting.

(15) Pain resulting from a forgotten fracture of a rib with callus pinching the nerve.

(16) Aneurism of the aorta.

(17) Obscure alleged neuralgias of the liver.

Objective Diagnosis.—Nothing unusual need be pointed out except as to the temperature. We have striking temperature ranges in hepatic disorder. One type to which Charcot first called attention is intermitting. This type, usually associated with ball-valve calculus, may be confounded with malaria (plasmodium), septicemia (blood cultures, streptococcus and gonococcus, or examinations of pus), endocarditis (same means of diagnosis), and recurring fever (Ebstein's disease) due to lymphatic tuberculosis (tuberculin test). It is this type of fever that is seen in syphilis, and such a cause must be excluded. Murphy calls attention to the rapid rise and fall of the temperature in gall-stone cases.

Physical Diagnosis.—The following methods secure valuable facts, and must be employed in each case:

(1) Inspection. Fixation or restriction of the side.

(2) Palpation. To find out if pain, tenderness, swelling, or spasm is present.

(a) Simple. Tenderness at Mayo Robson's point, at the juncture of the outer one-third with the inner two-thirds of a line drawn from the tip of the ninth right cartilage to the umbilicus. Outline tumor. If inflamed gall-bladder, continuous with the liver; if distended, movable, pear-shaped, neck toward liver having tendency to disappear and bob up again.

(b) Bimanual. Fluctuation. Gall-stone rubbing.

(c) Method of Glenard.

(d) Eight fingers. Pressure upon four fingers placed over the part by four of the other hand, the fingers of the hand not pressing being relaxed. (Pottalschek.)

(e) Hooking the fingers under the rib in the region of the gall-bladder or pressing deeply in this region while the patient takes a full breath. (Murphy.)

(f) Deep prod with the closed fist (Jordan-Lloyd) over the gall-bladder excites pain if gall-stones are present.

(3) Percussion. Outline tumor, note if continuous with liver. An interval of resonance may exist between the liver and gall-bladder tumors. Auscultatory percussion is not conclusive. Note,

however, that percussion must be employed in both the upright and the recumbent postures to detect displacements of the liver.

4. Auscultation. Friction of perihepatitis; gall-stone crepitus (rare).

X-Rays.—Of some value in the hands of Beck. Usually considered doubtful.

Exploratory Puncture.—Not justifiable.

Laboratory Diagnosis.—(1) *The Blood*.—(a) *Leukocytosis*.—It is remarkable how few reports are made. Fuller information is required on this important point. It is present in acute cholecystitis and cholangitis, not typhoid. Its presence points to streptococcus infections, to pneumococcus infections, to bacillus coli infections, and excludes typhoid, malarial, and tuberculous infections. It often excludes amebic abscess, but does not exclude multiple abscess of the liver. If lymphocytes are in excess syphilis is suggested.

(b) *Iodophilia*.—Locke and Cabot found positive reaction in five out of seven cases of disease of the gall-ducts. Their studies, however, showed positive results in a very large percentage of cases in which suppuration prevailed. One can place about the same value upon it as upon leukocytosis.

(c) *Red Blood Count*.—This should be made repeatedly. In jaundice it falls rapidly, and the degree of reduction should guide one in the indications for operation.

(d) *Coagulation Time*.—A close watch of the blood should be made with Wright's tubes. The normal coagulation time is from two to four minutes. In jaundice the blood may coagulate so slowly that eight to ten minutes may elapse before clotting is completed.

(e) *Tuberculin Test*.—Jaundice may be due to enlarged lymphatic glands pressing on the ducts. Recurrent fever (Ebstein's) attends it. It may simulate gall-bladder infections. A tumor of the liver so situated as to resemble an enlarged gall-bladder may be tuberculous. The test mentioned will give the characteristic reaction.

(f) *The Urine*. (From studies by Dr. Edsall.)—The presence of bilirubin indicates obstruction. Observers have long tried to find some indications from urinary analyses to distinguish the various forms of hepatic disease and differentiate between liver and gall-duct disease. My colleague, Dr. Edsall, has been engaged in these studies, has studied some of my cases, and I am permitted to give

his results—which, however, like those of others who have done similar work, are either negative or extremely inconclusive. They may, nevertheless, have some interest. His report is as follows:

“(1) The neutral sulphur of the urine was early determined to be increased in certain disorders of the liver. I estimated the neutral sulphur in a series of cases of liver disease with and without jaundice, in connection with some other urinary constituents. The results were very irregular and seemed to be of absolutely no consequence in diagnosis, as was to have been expected from the general physiological stand-point. Others have reached the same conclusion.

“(2) Recently (Edsall states) I have published some results of the estimation of the ‘readily eliminable’ fraction of the urinary sulphur. There was some reason to believe that this might bear an important relation to liver disease. My results, together with those of Petry and Lang, apparently demonstrate that this fraction of the urinary sulphur is of no clinical importance of any kind.

“(3) I have also made a considerable series of estimations of the ratio between the total nitrogen and the ammonia nitrogen of the urine in liver disease and in other conditions. This was of some interest, because of the teaching, which has so long been prevalent, that most of the urea is formed (from ammonia) in the liver. My results agree with those of others that have recently mentioned this question, in showing that this ratio has no importance in the diagnosis of hepatic disease, and indeed, it is all but certain that much of the urea is formed elsewhere than in the liver, particularly when that organ is diseased.

“(4) Since Strauss referred to some suggestive results from the estimation of the volatile fatty acids of the urine, I have made a series of estimations of these. I have repeatedly found excessive amounts in liver disease; I have quite as often found them normal; and I have frequently found them much increased, when there was no other indication of even temporary disturbance of the liver. Comparatively little work has been done on the excretion of the volatile fatty acids in various diseases, and more observations would be of value. I do not believe, however, that they will offer much aid in the diagnosis of disorder of the liver.

“(5) Strauss has also recently reported some very interesting results from tests for alimentary levuloseuria as a means of diag-

nosing disease of the liver; and Bruining and Ferrannini have had favorable results from the test. My own results in a small series of cases of cirrhosis have led me to believe that the test is of little or no practical value; for levulose did not appear in the urine of any of these cases in amounts sufficient to give a frank reduction of Fehling's solution or to cause distinct fermentation, and even the delicate Seliwanoff reaction was absent in half the cases. Moreover, this test is quite often positive in this slight degree in other conditions; then, too, it has no further experimental basis than the fact that Hans Sachs has shown that when the livers of frogs are removed, these animals do not assimilate levulose. It has never even been indicated that levulose is assimilated in frogs by the liver alone, or that this is so in any other animals. It is, indeed, extremely probable that other organs have a large share in this; hence, it is likely that liver disease has no constant or reliable relation to a disturbance in the assimilation of levulose.

“(6) I also began, some time ago, some work on the amidoacids of the urine in liver disease; but I have not carried this far. It was suggested by the recent work demonstrating the activity of autolysis in liver-substance, and by the well-known relation between acute yellow atrophy, etc., and the excretion of leucin and tyrosin. Von Jaksch has recently contributed a few observations related to this question, which are interesting. The matter would repay further study from a purely pathological stand-point, and perhaps from the clinical.

“(7) I have made numerous observations concerning urobilinuria, and can only agree with most other observers that it is, at most, suggestive of liver disease—and then, only when a number of other conditions can be reasonably excluded. The latter is a difficult task; and, further, urobilinuria is often absent in hepatic disease.

“It has been quite clearly established that urobilin is in most instances, at least, and in chief part, formed in the intestines by bacterial action. For this reason I have, with the aid of Dr. Fife and Dr. Wile, made a series of about 200 observations of the relations between urobilinuria and the excretion of various enterogenous decomposition products—a question that has hitherto received very little attention. A portion of these observations were made on cases that certainly had disease of the liver. The results indicate that

even in the absence of any demonstrable increase in blood-destruction, urobilinuria is not always dependent simply upon abnormal or increased intestinal decomposition-processes. Our results also lead me to think it probable that urobilinuria is commonly due to imperfect alteration of urobilin after its absorption from the digestive tract; and this imperfect alteration is probably due chiefly to disorder of the liver. This view is in accord with the growing opinion that excessive excretion of enterogenous decomposition-products often indicates disturbance in tissue-processes, rather than simply disturbance in the digestive tract. If this view can be demonstrated to be correct, it will indicate that urobilinuria is more directly related to disorder of the liver than is now generally taught; but more definite facts would be needed to give it greater diagnostic importance than it has at present.

"A number of observers have recently insisted that indicanuria is often an indication of disorder of the liver, rather than of the digestive tract. It is undoubtedly true that intense indicanuria, with or without urobilinuria, is often seen in liver disease, and frequently when any marked gastro-intestinal disturbance is absent. This is, however, an inconclusive fact, and one that offers no important aid in diagnosis.

"A fact that has interested me more than this is that I have repeatedly observed, in definite liver disease, and in chronic alcoholism when any distinctive signs of liver disease were, as yet, absent, that the distillate from the acidified urine persistently gave an intense phenol reaction (with bromin water), even when there were no noteworthy evidences of disturbance of the stomach or intestines. This intense phenol-reaction is common in infectious fevers and in marked gastro-intestinal disturbances. Except in such conditions, an intense reaction has, in my experience, been generally associated with disease of the liver, or with alcoholism or other conditions that gave rise to a suspicion of liver disease; and it has frequently been combined with a more or less marked urobilinuria. Herter has shown that liver-substance causes phenol to disappear, and it is also probable that the synthesis of phenol into conjugate sulphates takes place chiefly in the liver. These facts, the results that I have mentioned, and other reasons make it seem probable that phenol may bear some relation to liver disease that will prove to be of clinical importance. My observations concerning this point are,

as yet, very inconclusive. A mere excess of phenol in the urine is certainly not, of itself, in any way indicative of hepatic disease; but there are some features of the excretion of phenol that are, I believe, worthy of further attention in this connection."

(g) *Gastric Analyses*.—Such analyses carefully conducted will enable one to differentiate between liver and gastric conditions, and with the physical examinations will usually lead to the recognition of the gastropnoia and the dilatations which cause pain and simulate gall-bladder affections. It is well known that hyperacidity attends gall-stones. I found constant hyperacidity in two cases in young subjects who had symptoms of cholecystitis, but in whom I could not elicit the antecedent and attending phenomena of cholelithiasis. It occurred to me that as pancreatitis may be caused by hydrochloric acid, so cholecystitis might be induced if the acid could get into the ducts. Experiments conducted to determine this point by Drs. Yates and Pearce showed that in healthy subjects gastric juice could not be forced into the gall-bladder from the duodenum. The experiments were as follows:

(A) Two experiments—dead dog, pylorus ligated, duodenum below bile duct ligated. Bowel filled with eosin solution containing lamp-black in suspension. forcible manual pressure for several minutes. Result negative. Duct not stained.

(B) Same experiment on human cadaver. Result negative.

(C) Live dog. Ligation of duodenum 20 cm. below pylorus. Injection of same fluid. Animal killed after five hours. Had not vomited, but was collapsed, powerless, and in dying condition when chloroformed. Examination—slight eosin staining at papilla but no extension along duct.

(D) Same experiment, but ligation below the ileocecal valve. Dog killed after sixteen hours. Result negative.

Notwithstanding these negative results it may be possible that under altered pathological conditions hydrochloric acid or gastric juice may get into the bile passages and cause inflammation.

Historical Diagnosis.—Reliance placed on the age, sex, habits, and other facts of the social history, and of the previous medical history, is essential in the diagnosis of secondary states. A glance at the secondary morbid states explains this statement.

Fallacy.—Attention must be called to the fact that the age of persons suffering from cholelithiasis, as determined at autopsy or

in the operating-room, is not that at which the disease began. The age thus recorded is the age when the secondary processes of calculi have taken place, that is, infection of the biliary passages in which gall-stones are present, and produce the symptoms which require treatment or cause death.

REPORT OF CASES

CASE I.—*Acute Cholecystitis. Absence of Gall-Stones; Severe Infection. Operation. Immediate Recovery.*

J. R., aged 49 years, married. Resided in Philadelphia.

"Always reckless with eating" as to time, character of food, and method of eating. Moderate in the use of beer and whiskey. Passed a renal calculus several years ago. Always inclined to constipation and subject to so-called bilious attacks, which were relieved by purgatives.

Nothing further of interest in the social, family, or previous medical history.

On April 4, 1902, he partook of a supper of indigestible food. April 5, 4 A.M., he was seized with severe pain in the epigastrium and the hepatic region. His physician found him with pain, tenderness over the region of the gall-bladder, a temperature of 101° F., and a pulse of 106. There was no nausea, vomiting, or movement of bowels.

Pain continued during the day, for which morphin was taken. Unable to secure a movement of the bowels throughout the day.

April 6. Fairly quiet night under influence of morphin. Temperature 100° F., pulse 104. Pain increasing; abdomen very tympanitic, greatest tenderness over the gall-bladder region. At 4 P.M., the temperature was 103° F., the pulse 112. The bowels moved for the first time, after high enema. At 5 P.M., a rigor; pain continued. At 8 P.M., the rigor was repeated; temperature 103.8° F., pulse 116.

April 7. Poor night; moderate collapse; temperature 101° F., pulse 116. Sweating; great tenderness over the epigastrium and the gall-bladder. A palpable tumor in gall-bladder region. Seen by Dr. Musser. Diagnosis, acute cholecystitis. At 12 M., temperature 101.8° F., pulse 108. Nausea. No bowel movement. Otherwise same. Urine contained bile pigment; otherwise normal. At 5 P.M., the temperature was 102° F., the pulse 116. Much pain.

Operation declined. At 11 P.M., the temperature was 101.9° F., the pulse 124, the respiration 22. Pain; patient nervous and restless.

April 8. Very restless during night; very little sleep. Six stools, thin, yellow. Nausea. Temperature 101.4° F., pulse 110. Some perspiration during the morning. Headache and backache. Pain and tympany. At 2 P.M., temperature 102° F., pulse 98. At 5 P.M., temperature 105° F., pulse 120. Leukocytosis of 12,000.

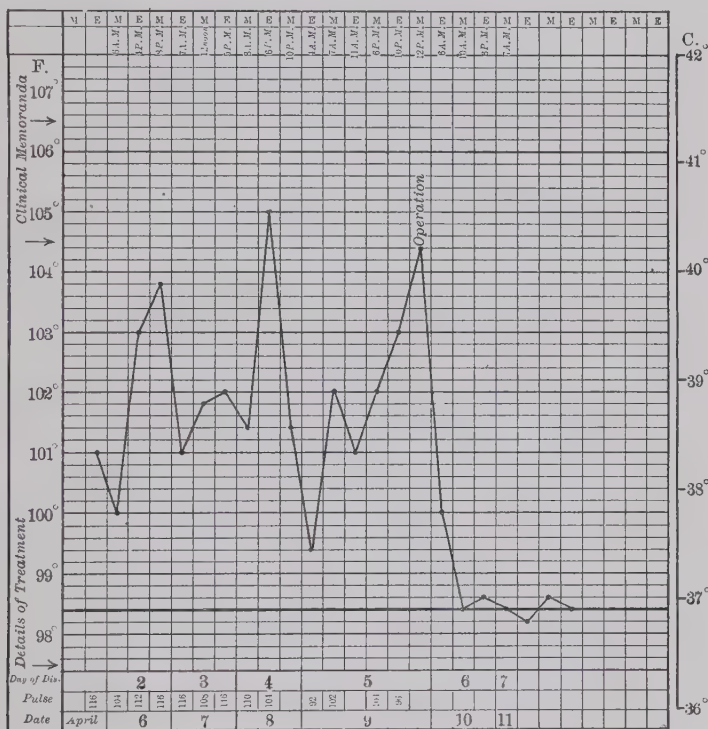


CHART I.—Acute cholecystitis. Operation. Recovery.

Backache and headache. Urine scanty and high colored. At 8 P.M., temperature 103.3° F., pulse 118. Thin, black stools during the evening. Local conditions the same.

April 9. At 4 A.M., temperature 99.4° F., pulse 92. At 8 A.M., temperature 102° F., pulse 102. Pain continues. Tumor distinct. At 12 M., temperature 101.2° F., pulse 96. Headache. At 3 P.M., local conditions more aggravated. Temperature 101.3° F.; pulse

100, respiration 28. Mild delirium; very short of breath. At 9 P.M., delirium increased along with other evidence of toxemia. Temperature 103° F., pulse 108, respiration 26. Throughout day several stools. Owing to manifest increase of toxemia and no relief to local symptoms, consent to operation, which Dr. Martin joined in advising, was given. Operation at 1 A.M. by Dr. Martin. Swollen, edematous gall-bladder surrounded by recent pericholecys-

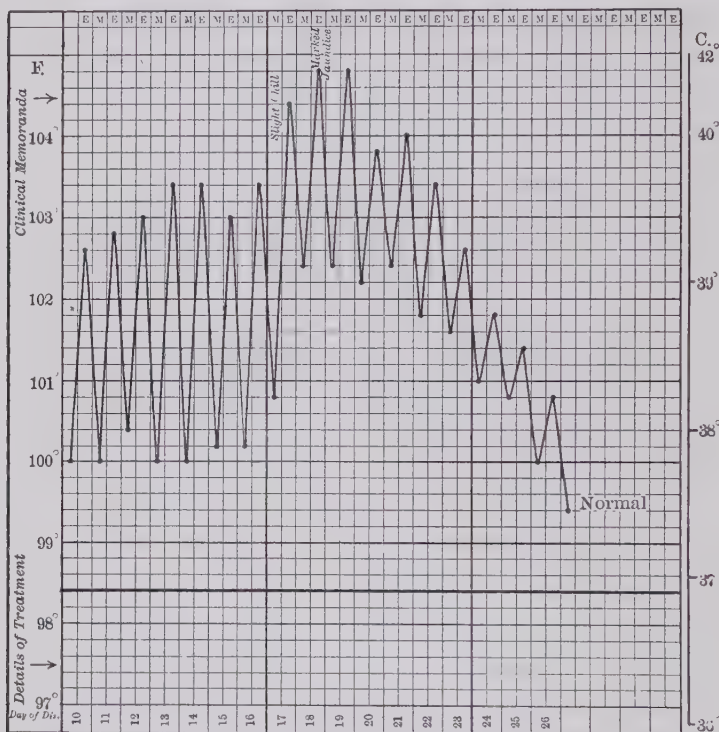


CHART II.—Cholangitis and cholecystitis in the course of typhoid fever.

titis. Distention due to enormous amount of seropurulent fluid. No gall-stones. Drainage. Immediate relief (see Chart I).

CASE II.—*Cholecystitis and Cholangitis in the Course of Typhoid Fever.*

February, 1903. In the third week, in the decline of the fever, of a moderately severe attack of typhoid fever, without any cause, increase of temperature developed, as shown in Chart II. At the end of four days I saw the patient in consultation. No unusual

symptoms. Slight nausea. Tongue furred. Marked, but not deep icterus. Tenderness of the gall-bladder, which was palpable. Liver not enlarged. Recovery in ten days.

CASE III.—*Typhoid Cholecystitis in Convalescence. Operation. Recovery.*

March, 1903. Patient, aged 55 years, married, female. Seen with Dr. Rehfuß. Typhoid fever of six weeks' duration. Four

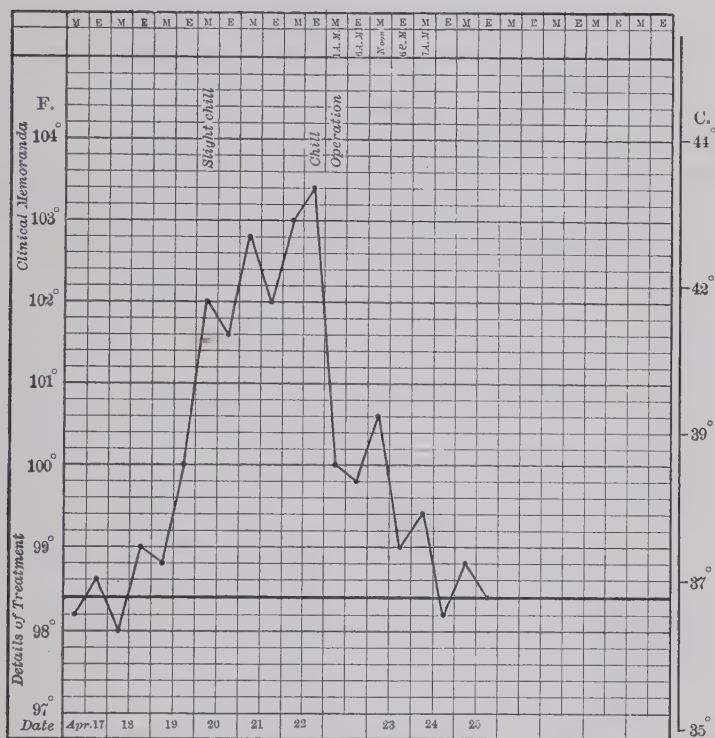


CHART III.—Cholecystitis in typhoid fever developing four days after the temperature reached normal. Operation. Recovery.

days after the temperature became normal she was seized with pain and vomiting. In the afternoon a chill occurred, and the temperature rose as shown on Chart III. The patient was seen by me on the third day, when tympany and tenderness in the region of the gall-bladder were present. The pulse was rapid and feeble. Constant vomiting. Bowels opened freely.

Physical examination indicated swelling, and the greatest ten-

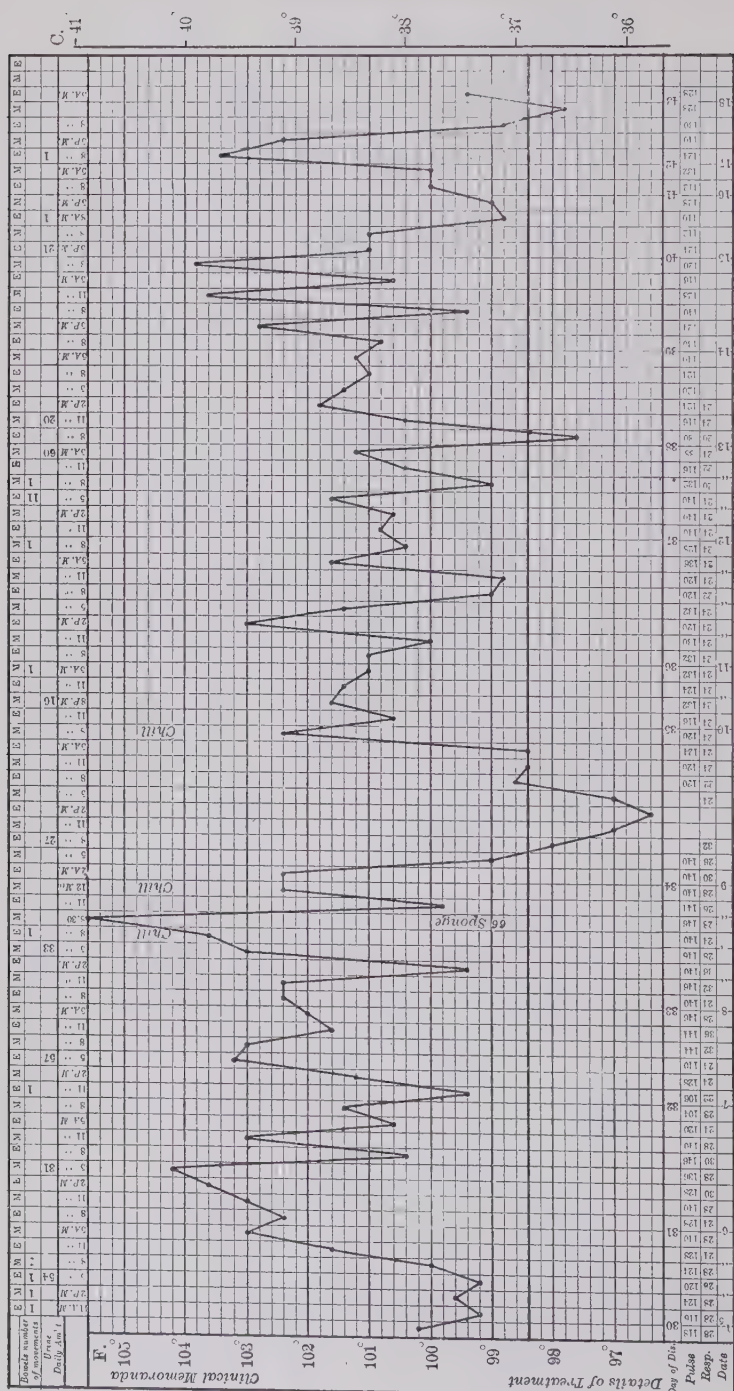


CHART IV.—Cholecystitis in typhoid fever developing forty eight hours after the temperature reached normal. Death from acute hemorrhagic pancreatitis.

derness was between the end of the ninth rib and the umbilicus. Rigidity of right rectus marked. Appendicitis was excluded because of the history and the location of pain and rigidity. Perforation was excluded because of the time in the course of the disease, because of absence of shock and sudden pain. It was evident that localized peritonitis was advancing rapidly to general. Dr. Martin concurred in the diagnosis and operated four hours after my visit, when the pulse was 160, vomiting constant, and tympany great. Very extensive peritonitis about liver, gall-bladder, and in right upper quadrant was found; the gall-bladder was enlarged and distended. It was opened and drained, with prompt recovery, as indicated by the chart.

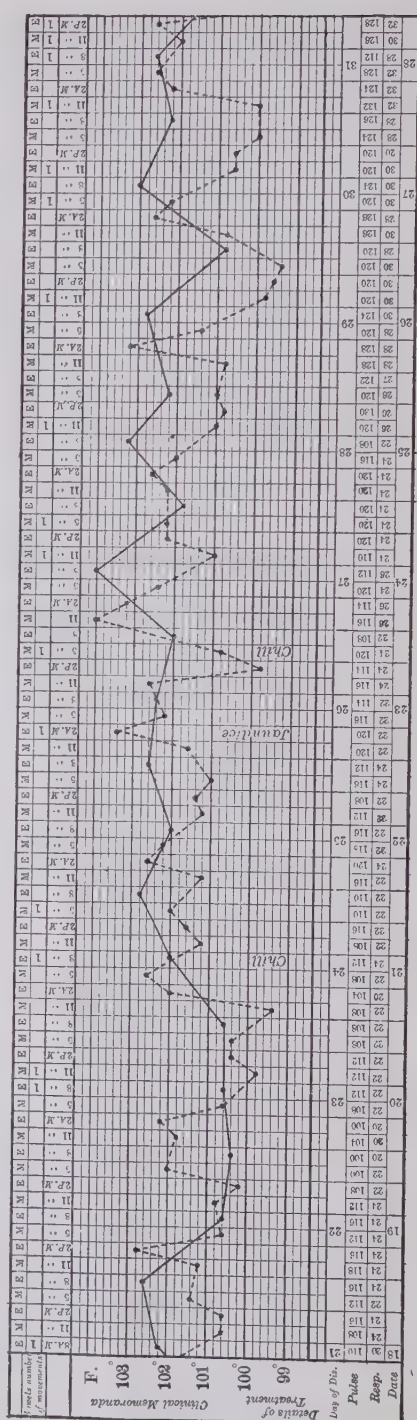
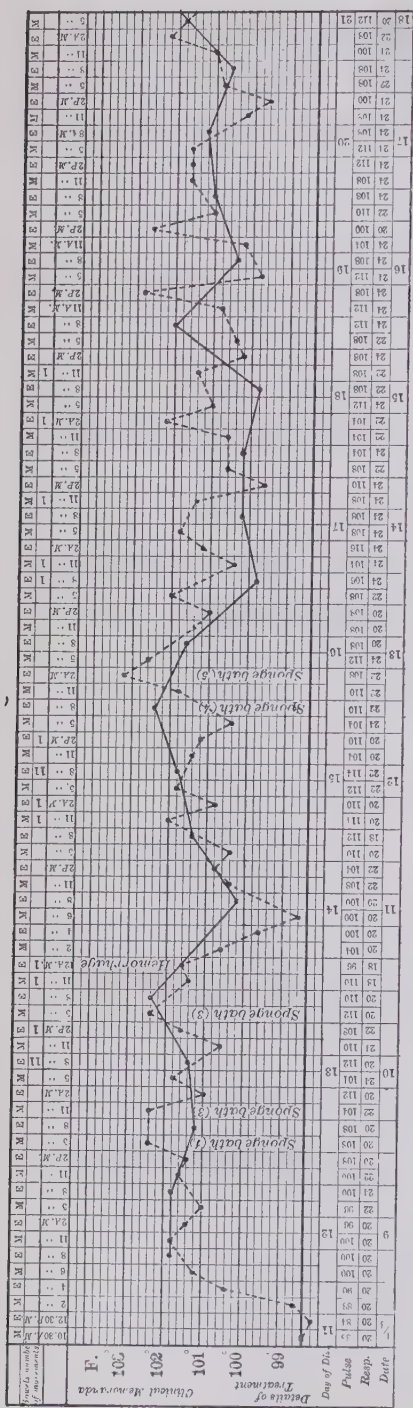
CASE IV.—*Typhoid Fever. Cholecystitis. Acute Pancreatitis. Death.*

January, 1903. The patient was desperately ill with typhoid fever for six weeks. The fever did not subside except for 48 hours. A recurrence of fever with chills, as Chart IV indicates, was believed to be due to ugly bed-sores and suppuration from hypodermoclysis abscesses. There were no signs of abdominal disease. One day, after slight exertion, turning to drink, she died suddenly.

At the autopsy, suppurative cholecystitis without gall-stones, and acute hemorrhagic pancreatitis were found. The great interest in the case is in the sequence of pancreatitis upon typhoid cholecystitis.

CASE V.—*Cholecystitis in the Course of Typhoid Fever. Recovery.*

The patient, a woman, aged 45 years, was seen in consultation with Dr. Taylor and Dr. Girvin, in 1901, on the twenty-fifth day of an attack of typhoid fever, on which day the temperature arose, and pain, rigidity, and tenderness in the gall-bladder region were found. A tumor the size of a large orange, movable with respiration, and on palpation tender, filled the region between the normal gall-bladder site and the umbilicus. The local symptoms were very severe for ten days, but gradually subsided, the temperature (see Chart V, pages 28 and 29) declining with the lessening of the abdominal symptoms.



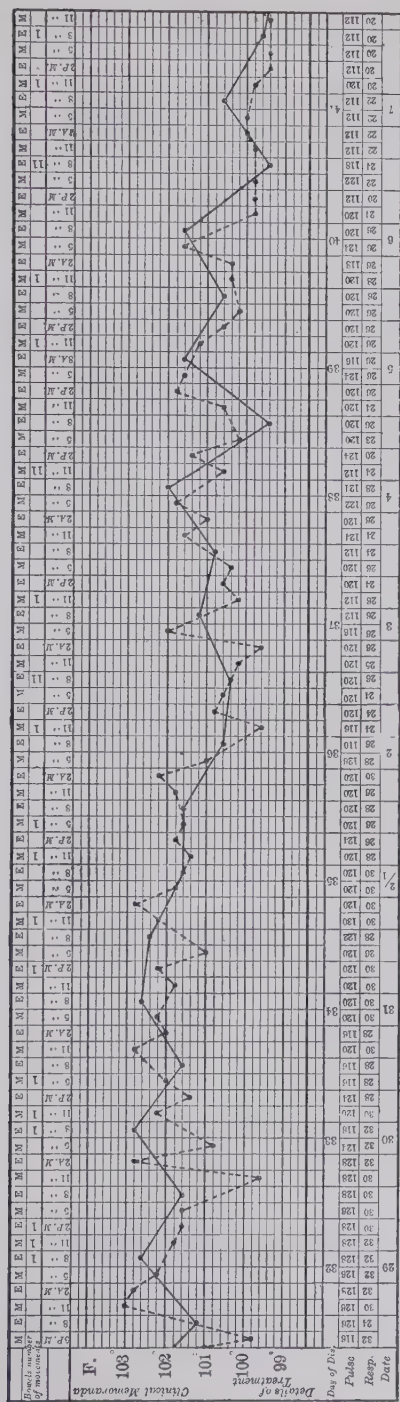


CHART V.—Cholecystitis in the course of typhoid fever.

THE CAUSATION, SYMPTOMS, AND DIAGNOSIS OF GALL-STONES

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CAUSATION

SOME of our knowledge regarding the etiology of gall-stone disease is certain, and a good deal is theoretical and subject to alteration from time to time, as new facts come to light. It may be as well to look first at the factors about which there is no doubt, and then to discuss shortly the more uncertain part of the subject.

Gall-stones seem to occur in all parts of the world and among all races and classes of people, the frequency with which they occur, however, being subject to great variation; thus, in Germany some 12 per cent. of all people have them; in the United States Mosher¹ found them in 6.94 per cent. of 1655 post-mortem records; in Russia they are rare (Djakonoff²); and in the East they are said to be very infrequent; and this is borne out by my own experience in India.

They occur much more frequently in women than in men, the proportion being given by different writers as anywhere from 3 to 1, to 5 to 1. Naunyn found them in 25 per cent. of all women over 60 years of age, and Shroeder's statistics show 20.6 per cent. of all women to have them. This is not the case, however, in America, as Mosher gives the proportion as 9.37 per cent.

Age is an important etiologic factor, gall-stones being very rare before adult life, and occurring most commonly after the age of 40. Cases, however, have been recorded of their occurrence in the newly-

¹ Bull. Johns Hopkins Hospital, 1901, xii, 253.

² Chiruragia, January, 1903.

born. Kraus,¹ in twenty-five years of practice at Carlsbad—during which he saw 2800 cases of gall-stones—never came across one in a patient under the age of 20; and then, by a curious coincidence, he saw five in one year. McPhedran, of Toronto, recently had a case of gall-stones in a woman of 25 years, in which a most distinct history of the disease had existed since the age of 12. Several stones were found in the gall-bladder at the operation.

The disease is said to be rarer in the poorer classes than in the well-to-do, and yet A. Dean Bevan² found that gall-stones occurred in 16 per cent. of his dissecting-room material, which would naturally be drawn from the lowest stratum of society.

Child-bearing no doubt exerts a very powerful influence in the production of the disease; and according to Shroeder, who compiled very extensive statistics of the disease, in Germany, Austria, and Switzerland, 90 per cent. of the females who suffered from the condition had borne children. Various diseases seem to have the same tendency; the most direct one in this respect being cholecystitis—to which reference will be made later. Typhoid fever frequently appears to produce the condition, as was first pointed out by Bernheim in 1899, and it is interesting to note that the typhoid bacillus may be in the gall-bladder for years, and the patient will give the Widal reaction years after the enteric fever itself has occurred. It does not at all follow, of course, that every case of gall-stone occurring after typhoid fever is due to that disease, and in some of the cases found in literature there is a distinct history of biliary colic occurring before the typhoid fever. C. N. B. Camac³ analyzes six cases of cholelithiasis following typhoid fever occurring in the Johns Hopkins Hospital, and concludes that "the typhoid bacillus aggravates cholecystitis in the presence of gall-stones, but that the typhoid bacillus is productive of gall-stones is by no means certain." According to Cushing,⁴ infection of the bile occurs in 50 per cent. of fatal typhoid fever cases, and this infection is apt, under certain conditions, to cause cholelithiasis.

¹ Beiträge zur Pathologie und Therapie der Gallensteinkrankheiten, Berlin, 1891, page 4.

² Annals of Surgery, 1902, xxxvi, 155.

³ Johns Hopkins Hospital Reports, 1900, viii, 339.

⁴ Hoppe-Seyler, Nothnagel's Encyclopedia of Practical Medicine (American edition, edited by F. A. Packard), page 541.

Heart disease seems to predispose to gall-stones. Brockbank¹ found gall-stones in 27 out of 49 cases of this disease. Probably the inactive life and the passive congestion of the liver and the gall passages which the cardiac disease engenders is the explanation of this association. The relation of gout and diabetes to gall-stones is interesting, and these conditions certainly seem to predispose toward their formation. It must be remembered that stout, elderly women are prone to both glycosuria and cholelithiasis. Cancer of the biliary passages is so frequently associated with gall-stones that it is often suspected of producing them. Zenker² found gall-stones in 85 per cent. of cases of cancer of the gall-bladder. Probably the stagnation of the bile and the frequently associated infection are the reasons. On the other hand, gall-stones seem to set up cancer in some cases, but with this phase of the subject we are not here concerned. The insane suffer more from gall-stones than do the sane. In 50 consecutive necropsies in the female department of the Colney Hatch Asylum, gall-stones were found in 18 cases, or 36 per cent.³

Nephritis was, of all diseases, the one most commonly found by Mosher to be associated with gall-stones, it being more or less marked in 72 per cent. of his cases. Occupation seems to exert some influence, and Kraus gives the following list of his own cases, occurring in different occupations: professors and teachers 103, officials 74, clergymen 60, physicians 45, tenants 41, merchants and bankers 40, military officers 40, small landowners 26, large landed proprietors 24, and manufacturers 19.

This list is, of course, open to many fallacies.

The influence of heredity is uncertain, as is also the effect of diet. Older authorities placed much more weight on the influence of diet than is now considered justifiable. "Experience has shown that in cases of biliary fistula, farinaceous and saccharine food will produce a dense, thick bile, whereas an albuminous diet will cause the biliary secretion to be more liquid. A dense, thick bile will act in the same way as stagnation in favoring the formation of

¹ On Gall-stones, London, 1896, page 55.

² Quoted by Moynihan, *British Medical Journal*, 1902, ii, 1530.

³ Beadles, C. F., *Journal of Mental Science*, 1892, xxxviii, 382.

calculi.”¹ If a farinaceous and saccharine diet had any great influence in the production of calculi, then one should find these very frequently in India, where a large proportion of the population subsist wholly on such a diet, and yet the very opposite is the case, these people being almost immune. They suffer largely from glycosuria and diabetes, but escape cholelithiasis.

Adiposity, especially abdominal adiposity, constipation, tight lacing, and sedentary habits, all predispose to the disease.

How do these diverse causes act in the production of calculi?

Biliary calculi are chiefly composed of cholesterin, a monatomic alcoholic body which occurs normally in very small quantity in the bile. The next most common body found in them is bilirubin calcium, the calcium salt of bile pigment. These two constituents occur in varying proportion, and thus one gets all grades of calculi, ranging from pure cholesterin to pure bilirubin. Naunyn divides them into six classes: (1) Pure cholesterin; (2) laminated cholesterin; (3) common gall-bladder stones; (4) mixed bilirubin calcium; (5) pure bilirubin calcium; and (6) rarer forms. The calculi formed in the hepatic ducts consist chiefly of bilirubin calcium; those in the gall-bladder are chiefly cholesterin. There are frequently foreign bodies and traces of other salts found in calculi, and in a large percentage of them, especially recently-formed ones, bacteria are found. The gall-bladder is the commonest situation for their formation, but they are also, as stated, formed in the hepatic ducts, and rarely in the cystic and common bile ducts. They are here found in elephants, in which animal no gall-bladder exists.²

The factors which may tend to cause precipitation of cholesterin in the gall-bladder are: (1) Increase in the percentage of cholesterin in the bile; (2) stagnation of the bile; (3) decrease in the normal solvent power of the bile for cholesterin; and (4) the presence of a nucleus.

(1) Mere concentration of bile does not cause gall-stones. The experiment has been tried³ of concentrating bile outside of the body by evaporation, and no concretions at all resembling calculi have been produced. The observations of Naunyn, confirmed by

¹ Graham, J. E., Sajous's Annual and Analytical Cyclopeda of Practical Medicine, 1899, ii, 196. Article "Cholelithiasis."

² Hoppe-Seyler, loc. cit., page 539.

³ Hoppe-Seyler, loc. cit., page 536.

Hunter, have shown pretty conclusively that at least most of the cholesterin of calculi is produced *in situ*, being secreted by the inflamed mucous membrane of the gall-bladder. Jankau and Thomas¹ have shown experimentally that diet has no influence upon the percentage of cholesterin in the bile, and Kausch² found that most diseases (apart from local biliary diseases) had similarly no effect. Cholesterin is found freely in many morbid secretions, as in that of bronchitis and in the contents of various cysts.

Gall-stones have been very frequently produced experimentally by mild infection of the gall-bladder with various germs; this has been done by Mignon, Fournier, Gilbert, Cushing, and others. They injected attenuated cultures of typhoid or colon bacilli into the gall-bladder, which produced cholecystitis with subsequent formation of calculi. Ligature of the cystic duct increases the effect of the injection. Last year Lartigan, at the meeting of the Association of American Pathologists, showed some very beautiful gall-stones which he had thus produced in rabbits. In support of the septic origin of gall-stones one may mention Mieczkowski's work. He found the bile in the gall-bladder sterile in all of 15 cases in which it had been obtained at operations for affections other than cholelithiasis. On the other hand, it was infected in 18 out of 23 cases of gall-stones.³ The occurrence of cholelithiasis after typhoid fever fits in well with these experimental results.

It is quite possible, however, that a non-bacterial catarrh may occur from various causes, such as the presence of chemical irritants in the bile, and thus it is not necessary to conclude that every case of cholesterin gall-stones is even indirectly due to bacteria. In 24 cases at the Johns Hopkins Hospital⁴ bacterial examination of the bile was made at the post-mortem, and in 11 it proved to be sterile. No special culture, however, was made to show the presence of the tubercle bacillus or the gonococcus. The colon bacillus was the one usually found. Of course it is possible, that, in all sterile cases, bacteria may have been present, caused the gall-stones, and then died out; but of this we have no proof. W. Hunter⁵ thinks that

¹ Quoted by Naunyn, *Klinik der Cholelithiasis*, Leipzig, 1892, pages 10 and 12.

² Quoted by Naunyn, *loc. cit.*, page 12.

³ Hoppe-Seyler, *loc. cit.*, page 540.

⁴ Mosher, C. D., *loc. cit.*, page 257.

⁵ *British Medical Journal*, 1897, ii, 1235.

the excretion of irritating substances through the bile, by causing a catarrh of the intrahepatic ducts, may produce the bilirubin calcium calculi. Gilbert and Fournier,¹ however, divided gall-stones into two groups: (*a*) Those due to the colon bacillus, and (*b*) those due to the *Bacillus typhosus*. Theoretically, infection of the gall-bladder and passages may come from above or below, but the weight of evidence is in favor of an ascending rather than a descending invasion. Fütterer² has shown, however, that in a few minutes after the injection of organisms into the circulation they appear in the bile.

(2) All authorities are agreed that stagnation of the bile is a very important predisposing cause of gall-stones. There is, in fact, considerable evidence that without it gall-stones cannot occur. It probably acts in a threefold manner: (*a*) By predisposing to bacterial invasion; (*b*) by encouraging the septic process after infection, just as retention of urine does, by allowing the bacteria to multiply and act undisturbed; and (*c*) by giving time for the sedimentation of the cholesterin or other constituents of the stones.

Stagnation *per se* does not produce precipitation of cholesterin in an aseptic gall-bladder, as has been proved by Mignon,³ who concludes that, "two causes are necessary for the production of gall-stones—the weakened micro-organism and stagnation of bile." "It is known that bile may remain for a long time in the gall-bladder,—as, for instance, in occlusion of the cystic duct,—and that this is followed by hydrops of the gall-bladder, but not by inspissation of bile."⁴ But it has been proved experimentally by Charcot, Naunyn, Netter, and others, that ligation of the common bile duct is followed by septic cholecystitis, and F. N. G. Starr and the writer showed recently that after this operation in dogs the retained bile soon swarms with bacteria. Probably occlusion of the common bile duct would be more apt to be followed by sepsis than stoppage of the cystic duct, as it has been frequently shown that the lower end of the normal common bile duct may contain bacteria,

¹ Nothnagel's Encyclopedia of Practical Medicine, Diseases of the Liver and Pancreas (Amer. Edit.), page 541.

² Quoted by Musser and Gwyn, Reference Handbook of the Medical Sciences, 1902, iv, 262.

³ Thèse de Paris, 1896.

⁴ Hoppe-Seyler, loc. cit., page 536.

while the gall-bladder does not normally do so. Many of the conditions which are known to increase the tendency to gall-stones act by producing stagnation, such as adiposity, sedentary living, female sex, tight lacing, etc. In the normal state the gall-bladder must fill and empty itself many times in the twenty-four hours, and this ebb and flow is carried out by the muscular coat and a very complete sphincter of non-striped muscle at the neck of the gall-bladder, these structures being governed by nerves. "Oddi has demonstrated this sphincter in different animals and in man, and L. F. Barker has been kind enough to prepare several specimens by his method which show the fibers very clearly. Doyon claimed to have discovered the biliary reflex—the afferent fibers pass in the vagus, and the efferent in the splanchnic—and states that stimulation of the central end of the vagus causes contraction of the gall-bladder, and at the same time relaxation of the sphincter choledochi." ¹ Now, in various sluggish conditions of the body, such as are engendered by an inactive life, adiposity, and various weakening diseases, etc., one can theorize with fairness on a want of tone in the muscular apparatus and inactive biliary reflex with a consequent stagnation of bile in the gall-bladder. "Charcot actually found that the unstriped muscle fibers in the walls of the biliary passages underwent very extensive atrophy in old people, and thus the cause of atony of old age was clearly demonstrated." ² Stagnation may also be brought about by pressure of tumors or adhesions about the gall passages, and such are frequently found at operations and post-mortems. A spasmodic condition of the biliary sphincter would act in the same manner and might lead to cholelithiasis, but of this we have no proof. Spasm of the bile passages is an accepted theory of the cause of emotional jaundice, and spasmodic conditions of various kinds are especially apt to occur in women about the menopause, that is, about the time when gall-stones are so often formed.

(3) The minute quantity of cholesterin normally present in the bile is kept in solution chiefly by the salts of the bile acids. Theoretically, if these salts should be diminished, cholesterin may be precipitated. The action of the bacteria in the bile is to make

¹ Quoted by Osler, *Lancet*, 1897, i, 1319.

² Quoted by Naunyn, *loc. cit.*, page 38.

it less alkaline, and this, no doubt, aids in the precipitation of the cholesterin when that, owing to the further action of the bacteria, is already there in excess. "Naunyn observed myelin globules within the degenerated epithelial cells of the biliary passages, and especially in the gall-bladder, which escape in a viscous condition and are seen floating about in the bile. On the addition of acetic acid, these masses solidify into a mass of cholesterin crystals. According to this view, then, the cholesterin of concretions has never been in solution in bile at all."¹

(4) Gall-stones usually form around nuclei. These may be masses of epithelial debris, inspissated mucus, small bilirubin-calcium calculi, foreign bodies of various kinds, or clumps of bacteria. Richardson, in a case of cholecystitis, found typhoid bacilli clumped "as if a gigantic serum reaction had taken place in the gall-bladder."² Aseptic foreign bodies experimentally introduced into the gall-bladder will not cause gall-stones (Mignon³).

The bilirubin-calcium calculi are formed chiefly in the hepatic ducts, and their formation differs from that of the cholesterin calculi. They are especially prone to occur when bile stasis from any cause is present, and in cirrhotic livers when the ducts are irregularly constricted. The salt does not occur normally in the bile at all. The mere increase in calcium intake, or even in the amount of calcium salts in the bile, does not lead to its formation. "What has been observed is, that the presence of albumin overcomes the retarding influence of bile salts on bilirubin-calcium formation, and it seems in all probability that this condition—that is, the presence of albumin in bile—is the deciding factor. Whether its presence is dependent on the disintegration of epithelium resulting from catarrh of the mucous surfaces, as was suggested by Naunyn, is not known, but it is not unreasonable to believe that at times albumin may pass from the blood through the hepatic cells into the bile, in much the same way as in nephritis it passes into the urine from the kidney."⁴ Hunter⁵ believes that this process is set

¹ E. E. Smith, Reference Handbook of the Medical Sciences, 1901, iii, 229.

² Journal of the Boston Society of Medical Sciences, 1898, iii, 79.

³ Thèse de Paris, 1896.

⁴ E. E. Smith, loc. cit.

⁵ Loc. cit.

up by the excretion of irritating substances in the bile, which cause a catarrh of the intrahepatic ducts in which these calculi are formed. The lime thus rapidly formed in the catarrhal process combines with the bilirubin to form a substance insoluble in bile. Small calculi thus formed may then escape and enter the gall-bladder and thus become nuclei for cholesterin deposit.

It is important to remember that gall-stones are usually multiple, it being quite exceptional to find only one. If they occur in the gall-passages, one or more is almost certain to be present also in the gall-bladder. In Mosher's series of 115 cases, in only 4 was the gall-bladder free from calculi when they appeared in other portions of the bile tract.¹ Their number varies from one to prodigious figures. Peters, of Toronto, found over 800 in a patient upon whom he recently operated; and E. E. Smith quotes one in which 7802 were present. As the cholelithiasis sometimes consists of mere sand, the actual number of grains is of little interest. The stones most to be dreaded are those which are too big to pass through the tubes except with difficulty, and yet sufficiently small to enter the cystic duct.

Gall-stones may recur after their removal, but this seems to be a rare occurrence, and symptom-producing cholelithiasis is seldom met with after previous operation for that condition. Riedel says definitely that stones do not recur, because the drainage cures the inflammation, and Kehr in a thousand cases saw no recurrence;² but many cases of recurrence have been recorded nevertheless. Homans³ reports one in which the gall-bladder was entirely emptied of stones in April, 1895, and in January, 1897, several round and oval calculi were found; sutures formed the nuclei of each. Kehr observed three such cases, in which silk sutures had dropped into the gall-bladder and led to renewed stone formation.⁴ Naunyn considers that there is much evidence that, in case a number of calculi are present in the gall-bladder, they have all been formed about the same time, and appear of the same age. He draws the conclusion from this that cholelithiasis is, as a rule, caused by one single infection, and that hence recurrences are rare.

¹ Loc. cit.

² Quoted by Andrews, *Annals of Surgery*, 1902, xxxvi, 157.

³ *Annals of Surgery*, 1897, xxvi, 114.

⁴ Gall-Stone Disease, 1901, p. 105; *Münch. med. Woch.*, 1902, xlix, 1689.

SYMPTOMS

Gall-stones, as a rule, produce no symptoms; it is the exception for their presence to be suspected. This is evident when one considers the frequency with which they are found post mortem, as compared with their being suspected during life. Kehr¹ believes that symptoms occur in only 5 per cent. of cases. Occasionally the first hint of the presence of cholelithiasis is intestinal obstruction produced by the calculus.

German writers describe two forms of cholelithiasis: the regular and the irregular; the latter meaning gall-stones plus complications. The former only, or regular cholelithiasis, can be at all fully dealt with here.

The great majority of gall-stones, as has been seen, are formed in the gall-bladder, and there they remain. In many cases, no doubt, some are passed on into the bowel without producing symptoms, these being of much less diameter than the lumen of the ducts. In other cases the calculi are so large that they cannot enter the cystic duct at all, and such will not likely produce serious trouble. It is the moderate-sized calculi, those that can enter the ducts and yet cannot pass through them without difficulty, that are to be dreaded. Kraus² and Cyr have described a prodromal stage of cholelithiasis, in which the patient suffers from gastro-intestinal symptoms and ill health, with some tenderness on the right side, and slight jaundice. Naunyn³ says that "in this description I recognize merely the manifestations of chronic dyspepsia," and with this it is difficult not to agree.

Do gall-stones lying free in the bladder produce any symptoms at all? In most cases, as has just been said, the answer must be in the negative, but sometimes they do. They are foreign bodies there, and by their presence are apt to damage the mucous membrane, and thus predispose to cholecystitis, and hence to symptoms of that disease. If such a patient, for example, should suffer from typhoid fever, the tendency to infection of the gall-bladder will be much increased. Moreover, calculi in the gall-bladder may occasionally give rise to a dragging feeling in the side, often worse after meals,

¹ Loc. cit., page 25.

² Loc. cit., page 14.

³ Loc. cit., page 51.

or to a sensation of weight there; and in nervous subjects they can act as a reflex source of irritation which may set up various neurasthenic symptoms. Such results of calculi in the gall-bladder are probably exceptional. If cholecystitis occur, it may, and frequently does, produce local peritonitis with adhesions around the gall-bladder, and probably these adhesions are often the cause of the vague dragging pains complained of. Such adhesions may even constrict the pylorus. Hale White¹ has recently emphasized the importance of these complications.

The symptoms of gall-stone are usually due to the presence of a calculus in the ducts, with attempts on the part of the ducts to force it onward into the bowel. The classical symptoms are: pain, with signs of shock; jaundice; fever; and the discovery of calculi in the feces. Cullen's definition was: "*Icterus cum dolore in regione epigastrica, acuto, post pastum aucto, et cum dejectione concretionum biliosarum,*" but very often many of these symptoms may be absent, and the diagnosis is difficult or impossible. We may consider these symptoms in detail.

Jaundice.—This will nearly always occur when the stone lies anywhere in the direct route between the liver and the bowel—that is, in the hepatic ducts or the common bile ducts. After the occurrence of colic, jaundice will usually appear in from 8 to 12 hours, and bile may be detected in the urine a good deal sooner than this. The stools at the same time will show bile to be more or less absent from them. If the stone have passed into the bowel, the jaundice will slowly disappear, but may take some days to do so. Probably the mechanical irritation produced by the calculus in transit sets up in these cases a cholangitis, which causes an obstructive jaundice in the wake of the calculus. When a more permanent impaction occurs, the jaundice becomes intense, and the patient may soon die of cholemia. The human body shows great variation in the degree of cholemic poisoning which it can endure, some individuals being very easily poisoned, whilst others are not so. W. T. Cocking² records the case of a woman who had been deeply jaundiced for fifty years. He considered it to be one of congenital stenosis; the gall-

¹ British Medical Journal, 1903, i, 537.

² Quarterly Medical Journal for Yorkshire and Adjoining Counties, 1902-3, xi, 104.

bladder could be felt as an elongated tumor. Sometimes the icterus is slight, or even absent, and it may vary greatly from time to time. In such cases either the irregular form of the stone permits of the partial flow of bile past it, or the calculus lies free in the diverticulum of Vater.

The variation in the degree of jaundice may be due to "the ball-valve" action of the stone, however, or to the varying amount of the swelling of the mucous membrane set up by its presence. The jaundice may vary also in a given case from a fluctuation either in the production of bile, or in its reabsorption, or lastly, in its rate of removal from the blood by other organs. To these last causes only can be attributed the variation in the degree of jaundice which one sees in cases of cancer of the gall-passages. More or less, sometimes intense, pruritus accompanies the icterus, and this itching may be the symptom most complained of. It does not always depend upon the degree of jaundice, being occasionally most marked when the tint is not particularly deep. Accompanying the bile stasis there is usually some enlargement and tenderness of the liver. The gall-bladder may be distended and easily palpable, but more commonly that viscus is shrunken from old cholecystitis.

Pain.—This is of two kinds: (a) More or less constant, and (b) colic. The former may vary from mere discomfort about the right side to severe aching, gnawing, or dragging pain. It is usually more or less present when the calculi are in the ducts. It is probably chiefly inflammatory in character and due to the infective cholecystitis or cholangitis, often with ulceration of the mucous membrane set up by the presence of the stones. Along with this pain there is frequently tenderness over the liver. Very often tenderness is best marked at two special points: (1) At a spot about midway between the ninth right costal cartilage and the umbilicus; and (2) immediately to the right of the eleventh and twelfth dorsal spines (Boas's point).

Biliary colic is usually sudden in onset, and indicates the presence of a calculus in the bile-passages, with attempts on the part of the muscular structures to force it onward. Occasionally the colic commences gradually with yawning and shivering. It varies greatly in acuteness, and frequently is of such intensity as to produce a severe degree of shock. Such shock may be fatal, as in three cases recorded by Murchison. In people who have had many

attacks of colic, and especially in the aged, these symptoms may be little marked; in any case, individuals seem to vary greatly in the amount of pain produced by the passage of gall-stones. The pain varies from minute to minute, as all colics do, increasing probably as the peristaltic waves pass over the muscular coat of the biliary structures. It is nearly always accompanied by vomiting, and this so often relieves in part the agony, that patients who have suffered before frequently endeavor to produce it. The vomiting may be very severe and may persist after the stone has reached the bowel. It may even produce death, as in a case mentioned by Mayo Robson.¹ The general symptoms of shock are more or less present—cold extremities, sweating, pallor of the surfaces, with depressed circulation. Usually, after an uncertain duration, the agony suddenly ceases, due to the delivery of the stone into the bowel, or its less likely dropping back into the gall-bladder; but a dull aching may remain for some time. Occasionally, however, the symptoms of colic gradually and only partially disappear—become remittent—and then the calculus has remained in the passages, where it may stay for years. Probably the pain lessens or ceases from time to time because the muscular coat of the biliary structures becomes tired out, as may occur in the parturient uterus when labor is prolonged. It should be mentioned that Kehr² believes that stones in the bile-passages do not produce pain until infection is added, when the resulting exudate dislodges them into the other parts of the ducts, producing the symptoms of biliary colic. Riedel endorses this view. Kraus³ believes that within the liver it is simply the flow of bile which forces stones on, while in the bladder and the larger ducts it is muscular action.

In the “ball-valve” type of disease, in which the stone lies freely in the ampulla of Vater, the pain may be periodical, slight, or even absent, and the condition declares itself more by the varying jaundice and fever.

The stone is first forced out of the gall-bladder by the muscular contraction of the wall of that viscus, and hence anything which tends to excite such contraction is apt to precipitate an attack of

¹ Clifford Allbutt's System of Medicine, iv, 238.

² Loc. cit., page 28.

³ Loc. cit., page 18.

biliary colic, or will make it worse when it already exists in chronic form. Now, the gall-bladder normally empties itself two or three hours after a meal, at the time when the chyme passes into the duodenum from the stomach; and clinically it is found that at such times, and especially at night, colic is specially apt to occur. Other factors which may precipitate an attack are violent movements, emotions, or the taking of certain articles of diet—all probably acting by setting up reflexly contraction of the gall-bladder.

Fever.—The presence of gall-stones in the gall-bladder will not produce fever in uncomplicated cases. When an attack of biliary colic occurs, there is usually an accompanying rise in temperature, even when the surface and extremities feel cold. This type is probably reflex in nature. Kraus, however, believes that the temperature is usually normal or subnormal during such an attack. When impaction of some duration occurs, fever nearly always occurs, and is of an irregular, intermittent type, with rigors and sweating. Charcot called special attention to this type of fever, and it usually goes by his name. It is probably chiefly septic in character, due to absorption of the dammed-up, septic, biliary contents, while absorption may be increased by ulceration of the mucous membrane. Mayo Robson¹ considers that it may be both nervous and septic. Murchison thought it was nervous, and corresponded to the fever occasionally caused by the passage of a urethral catheter. Mere partial retention of bile does not seem to be sufficient cause, and Osler records two cases of stenosis of the common duct in which there was no fever. The intermittent type of fever with varying jaundice is especially suggestive of a calculus in the ampulla of Vater, as has been emphasized by Osler.²

The finding of biliary calculi in the stools is, of course, conclusive evidence of cholelithiasis, but it is necessary to make sure that such excretions thus found are really of biliary origin. Foreign bodies of various kinds and intestinal concretions are apt to cause mistakes here. Usually the calculus will appear in the dejections within a day or two of the colic, but may not do so so soon. Calculi seldom float, as was once supposed to be the case. In searching for them the motions should be rendered fluid with water, and then

¹ Clifford Allbutt's System of Medicine, iv, 239.

² Lancet, 1897, i, 1319.

carefully strained through muslin or a fine sieve. In spite of the greatest care they may not be discovered, because they have become broken up and dissolved in the bowel. Naunyn¹ administered several gall-stones by the mouth, and in spite of a most diligent search did not succeed in recovering all of them from the feces.

DIAGNOSIS

From what has been said, it is evident that in most cases gall-stones cannot be diagnosed, because they give rise to no symptoms during life. In a few cases indefinite symptoms of dragging pain and discomfort may lead to a suspicion of their presence in the gall-bladder, and then physical examination may confirm their presence.

It cannot be too strongly urged that in every case a careful and complete inquiry should be made into the whole history of the case, and upon this and the general state of the patient more reliance can usually be placed than upon any physical examination short of an exploratory incision. The older physicians paid more attention to this point than is done now, very greatly to their advantage.

The x-ray has not proved of much service, owing chiefly to the fact that cholesterin concretions are permeable by the ray. Beck,² of New York, has, however, succeeded, after many difficulties, in getting some good skiagraphs.

As already mentioned, local tenderness may often suggest gall-stones, especially at two points,—(a) midway between the ninth right costal cartilage and the umbilicus, and (b) immediately to the right of the eleventh and twelfth dorsal spines (Boas's point). This latter sign was well illustrated in one of McPhedran's cases recently.

The conditions most apt to be confounded with gall-stone are the following: Intercostal neuralgia, gastralgia, ulcer of the stomach and duodenum, appendicitis, hepatalgia, pancreatic calculi and tumors, renal colic, movable kidney, tumors of the gall-bladder and biliary passages, suppurative cholangitis, and malaria.

Intercostal neuralgia can usually be easily excluded by the absence of jaundice and fever and the presence of definite tender points along certain intercostal nerves; but, as Trousseau pointed

¹ Loc. cit., page 76.

² American Medicine, June 22, 1901.

out, it may complicate gall-stone; and probably Boas's point of tenderness is thus explained.

Gastralgia usually occurs before middle life, when gall-stones are rare; there is no jaundice or fever; the pain is more to the left, and is usually relieved by food, often by firm pressure. Frequent mistakes are made here, usually in the direction of mistaking gall-stone for gastralgia.

Ulcer of the stomach and duodenum (the former at least) usually occurs in young women; the pain is quickly made worse by food; and the vomited matter contains blood, which may also occur in the stools. In neither is there any jaundice.

Hepatalgia is a rare affection, and its existence is doubted by many. Kraus¹ never saw a case, nor did Murchison. There will be no jaundice, vomiting, or fever.

Pancreatic calculi may produce symptoms hard to distinguish from those of gall-stones. Minnich² reports a case in which a patient who had suffered previously from cholelithiasis due to typical pigmented gall-stones found in the stools, could not distinguish these attacks from those in which concretions, apparently pancreatic, were discharged. The pain is apt to be toward the left, and jaundice is rare, although it may occur when the impaction is near the exit of the duct of Wirsung, as in a case recently quoted by Sydney Phillips.³ Glycosuria is apt to be present. The dejections contain abundant fatty acids, an excess of undigested muscle fiber, and sometimes the characteristic carbonate of lime calculi. It is said that pancreatic obstruction prevents carbouluria when salol is administered by the mouth. Sydney Phillips doubts the value of this test.

Appendicitis.—Here the pain and tenderness are usually below the level of the umbilicus, and a swelling can usually be made out there. There will be no jaundice, except in secondary septic conditions of the liver. Leukocytosis will be present, which will not be the case in gall-stones unless there be associated inflammatory complications.

Renal Colic.—The pain, which in its nature may closely resem-

¹ Loc. cit., page 39.

² Berl. klin. Woch., 1894, xxxi, 187.

³ Lancet, 1903, i, 1796.

ble that of biliary colic, is lower down, and radiates downward toward the genitals. There is no jaundice, and usually urinary symptoms are present.

Movable Kidney.—Here mistakes have often been made, especially in the direction of taking this condition for gall-stone. The movable kidney may drag or press upon the common bile duct so as temporarily to obliterate its lumen, and then biliary colic occurs, with jaundice and vomiting. The discovery of a floating right kidney does not exclude gall-stones, as the two conditions may coexist. It may be added that a distended gall-bladder and a floating kidney are often hard to differentiate, and the keenest clinicians make mistakes here. Treves and Maclagan¹ report three cases of floating kidney in which gall-stone colic was simulated. Pain, jaundice, and fever were present in each case. At the operations the kidney was found pressing directly upon the bile-passages. In all, complete relief resulted from fixation of the offending kidney.

New growths, especially malignant tumors of the gall-passages, may be difficult or impossible to distinguish from cholelithiasis. The two conditions may coexist, and both are specially apt to occur in elderly women. Mayo Robson² believes that such new growths and gall-stone can scarcely ever be differentiated, although in some cases the absence of pain and the rapid deterioration of health may suggest the more serious condition. In cancer the jaundice will likely be more constant, and the fever less or absent. The presence of a distended gall-bladder is decidedly in favor of cancer, as in cholelithiasis it is usually smaller than normal, the accompanying cholecystitis having produced a shrinkage here.

Suppurative cholangitis may be suspected when the condition is really one of calculus in the diverticulum of Vater, and indeed both may be present, as in a case which recently occurred in the practice of Hugh Macallum, of London, Ontario. Leukocytosis, profuse sweating, and much tenderness will be in favor of the presence of this condition.

Malaria.—Osler mentions that nearly all his cases of ball-valve cholelithiasis had been diagnosed before admission as cases

¹ Lancet, 1900, i, 15.

² Clifford Allbutt's System of Medicine, iv, 242.

of malaria. In any doubtful case the examination of the blood for the malarial parasite should settle the point.

THE SITUATION OF THE CALCULUS IN THE BILE STRUCTURES is of great importance and may often be diagnosed:

In the Gall-Bladder.—Enough has been said of their presence in the gall-bladder. If the concretions are large or numerous they may occasionally be felt in the gall-bladder. In a few cases deep palpation will cause a grating of the stones, the one against the other, feeling, as Murchison says, “like the grasping of a bag of hazelnuts.” Anders ¹ has lately specially called attention to the value of this sign. Palpation of a calculus-containing gall-bladder is, however, not free from risk. Still more risky is the use of an exploratory needle, which is now almost universally condemned, owing to the danger of infecting the peritoneum.

In the Hepatic Ducts.—The calculi which occur here are, as a rule, the bilirubin-calcium form, and they usually pass on without difficulty while small, owing to the fact that the caliber of the ducts gets steadily greater. They may go right on to the bowel or enter the gall-bladder and there form nuclei for larger stones. Occasionally, however, they become impacted in the hepatic ducts, and then may produce symptoms. If the impaction occurs in any of the radicles, there may be pain and intermittent fever without jaundice. The pain is indefinite, but situated about the hepatic region. The gall-bladder will not be enlarged. Thudichum ² thought that intermittent fever without pain or jaundice was suggestive of calculi in this situation. Occasionally so many of the hepatic ducts may be plugged by concretions that few remain patent, as in a case related by Chopart (quoted by Murchison); ³ in such a case it is easy to see that obstructive jaundice might occur. When the hepatic duct itself is the site of the impaction (a very rare occurrence), pain, jaundice, and fever will be present without enlargement of the gall-bladder.

In the Cystic Duct.—Very commonly the calculus becomes impacted here, in the cystic duct, whereupon it sets up pain and fever

¹ International Medical Magazine, 1899, viii, 881.

² Treatise on Gall-Stone, London, 1863, page 222.

³ Trans. Path. Soc. Lond., 1870, xxi, 221.

without jaundice. Murchison, Naunyn, Hoppe-Seyler, and most others, agree as to the absence of jaundice in such cases, and theoretically, it seems that this should be; but Kraus believes that jaundice occurs in from 10 to 20 per cent. of such cases.

In the Common Bile Duct.—The two narrowest parts of the bile-passages are the beginning of the cystic duct and the end of the ductus choledochus. The result is that the calculi formed in the gall-bladder usually never leave that viscus, but if they do so they are most apt to travel down and become lodged in the lower end of the common bile duct. After a few hours of agony they usually force a passage into the bowel. This may not occur, however, and they may remain more or less permanently in the duct, when jaundice, fever, and all the other symptoms of gall-stone mentioned will most likely be present. The gall-bladder will probably be small. Ecklin¹ found that in 172 cases of obstruction of the common bile duct from calculus, in 34 the gall-bladder was normal, in 110 it was contracted, and in 28 enlarged. In 139 cases of obstruction due to other causes, in 9 it was normal, in 9 small, and in 121 it was dilated. The tender area midway between the ninth right costal cartilage and the umbilicus is most apt to be present when the impaction is in the common bile duct. The classical picture of gall-stone loose in the diverticulum of Vater, so well described by Osler, has already been mentioned. The symptoms are, as quoted from Naunyn: Continuous or occasional presence of bile in the feces; distinct variation in the intensity of the jaundice; normal size, or only slight enlargement of the liver; absence of distention of the gall-bladder; enlargement of the spleen; absence of ascites; presence of febrile disturbance; and duration of the jaundice for more than one year.

The diagnosis of regular cholelithiasis is full of surprises, and in difficult and distressing cases an exploratory incision is often justifiable. The irregular forms of the disease—cholelithiasis plus complications—are often still more difficult to detect, and these complications may constitute the condition complained of, the original cause having disappeared or become masked. A good list of these complications is given by Mayo Robson.²

¹ Quoted by Osler, loc. cit., page 1322.

² Clifford Allbutt's System of Medicine, iv, 240.

THE DIAGNOSIS AND MEDICAL TREATMENT OF CHOLELITHIASIS AND CHOLECYSTITIS

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It is generally held that an important, if not necessary, feature of the etiology of cholelithiasis is to be found in a disturbance of the epithelial lining of the gall-bladder. Given a perversion of the nutrition, and exudation from the lining, of this viscus and the formation of biliary calculi may be expected. A mass of evidence has accumulated which goes to show that in the majority of instances the disturbance in the lining of the gall-bladder is most commonly brought about by the entrance of bacteria into the organ and the setting up of a mild or severe cholecystitis. Statistics show that there are certain predisposing factors of importance, among which are age, sex, indolence, gluttony, and constipation. The disease is most often observed in stout, constipated, inactive women of middle age, or older. So closely associated is cholelithiasis to cholecystitis, both in the matter of etiology and clinical history, that the diagnostician must necessarily consider both processes, and it is not always easy to separate the phenomena depending upon the one from those depending upon the other. In acute inflammation of the gall-bladder occurring in typhoid fever, with the presence of a pure culture of Eberth's bacillus, we have perhaps the most classic instance of uncomplicated cholecystitis; and yet in operating for the relief of this condition, newly-formed and relatively soft gall-stones, containing living typhoid bacilli, are sometimes found. In chronic cases following this infection, calculi are almost invariably present. Naturally the personal history of the patient as to age, activity, habits of life, and previous infections has some bearing in the diagnosis.

Acute cholecystitis usually gives rise to distention of the gall-bladder with either serous or purulent fluid. This accumulation of fluid depends upon the closure of the cystic duct as a result of

inflammatory swelling, and the pouring out of an inflammatory exudate more or less rich in the cellular elements of the blood and the epithelium of the gall-bladder, depending upon the activity of the process. The affection is accompanied by local and constitutional phenomena. Locally there is increased tension, and the soft parts in the vicinity acquire an increased rigidity. The gall-bladder may protrude below the liver, and may be palpated as a rounded mass continuous with the right lobe of the liver, which latter is usually somewhat enlarged. Not infrequently there is an accompanying localized angiocholitis, in which case there is likely to be also a more or less active and extensive pericholecystitis with adhesions. The region is tender, painful, sometimes showing prominence upon inspection, and it is to be noted that the process occurs along the lower rather than the upper border of the liver, and affects the right lobe rather than the left. The pain is sometimes very severe, sometimes only moderate, but is rarely altogether absent. There is usually continuous suffering, augmented by paroxysms of severe pain like the pain of biliary colic. The disease is accompanied by fever, usually with rigors, or even severe chills, occasionally attended by marked remissions and sweating; as a rule there is vomiting, often constipation with moderate tympanites, at times accompanied by jaundice with its special symptoms. A leukocytosis is to be expected, and I have known the white cells to rise to 25,000 or 30,000 a cubic millimeter, even when pus was not present. The patient is sometimes gravely ill, and the destructive processes are so active that drainage by surgical intervention is necessary to save life. In other cases the inflammation subsides—to recur, perhaps repeatedly. Sometimes during the periods of improvement numerous small, soft biliary calculi are passed by the rectum.

From this description it will be seen that it is impracticable to differentiate between acute cholecystitis with and without cholelithiasis, and it is not always possible to distinguish between a purulent and a non-purulent case. Sometimes the obstruction of the cystic duct is relatively permanent, in which case there may result either hydrops of the gall-bladder or empyema of the gall-bladder. The development of either of these may be recognized from the large, elastic, rounded tumor, occurring in the abdomen, below the right lobe of the liver. In the absence of acute inflammation one would not expect to find a leukocytosis except when the

contained fluid is purulent in character; but when the active inflammation has subsided, the leukocyte count cannot be depended upon as a positive guide, for then, even in purulent cases, the count is sometimes not very high.

Mild or subacute cholecystitis, while less frequently described by authors, must be a condition which often occurs and which undoubtedly is often overlooked because the signs and symptoms are inconspicuous. One has the opportunity of studying the condition in cases which have begun as acute processes but in which the inflammation has subsided. Here the severe pain and tenderness, the fever, digestive derangement, and other symptoms, markedly subside and some of them entirely disappear, but enough remain to hold the attention when once directed to the diseased part. The liver sometimes returns to its normal size, but usually is slightly enlarged, especially in that part of the right lobe lying immediately over the gall-bladder. This portion of the liver sometimes still further enlarges and extends downward in a "tongue-like projection," the so-called process of Riegel. It generally may be found when gall-stones are present and when the local irritation is considerable and protracted. Under these conditions the gall-bladder itself is likely to shrink from inflammatory thickening and subsequent contraction of the walls, and therefore is no longer palpable. Still one finds cases in which the gall-bladder remains large, extending below the liver, even when the right lobe is increased in bulk. In such cases the walls of the gall-bladder are usually thin, and the tumor may appear elastic upon palpation. A gall-bladder which has once been inflamed is often adherent to the liver, the omentum, or the intestine.

These persistent adhesions may give rise to a special train of symptoms. When the adhesions extend to the abdominal wall, there may be a sense of tension or even pain when the patient assumes the upright position. When attached to the pylorus they may give rise to important symptoms which are most marked toward the completion of the gastric digestion, when the pylorus is most active, and there may result symptoms of food stagnation, uneasiness, pain, a sense of distention, eructation of gas, water-brash, ending with nausea and vomiting. Symptoms resembling the above-named sometimes result from adhesions to the duodenum. In some instances of adhesions the symptoms are less localized, and there

is found to be a vague disturbance of the entire digestive tract with accompanying auto-intoxication, constipation, diarrhea, or other digestive derangements. The diagnosis of these adhesions is not always easily made, especially when no evidence of disease of the gall-bladder can be made out by physical examination. A correct diagnosis is sometimes to be made by exclusion and by bearing in mind the fact that the symptoms develop subsequent to an attack of recognized cholecystitis. An intercurrent attack of biliary colic, when it occurs, will assist one materially in reaching a correct conclusion.

When chronic irritation—varied by periods of mild inflammation—of the gall-bladder exists it may produce other symptoms that assist in the diagnosis. In some cases there is a subicteric appearance of the skin and conjunctivæ, often transient, which betrays the existence of occasional attacks of mild angiocholitis. Some patients experience repeated attacks of distinct jaundice. During the period of irritation there is a sensation of weight, or even pain, in the right hypochondrium or epigastrium, tenderness at the juncture of the ninth rib and cartilage, and sometimes at the point of the twelfth right intercostal nerve, an inch from the spine. This, the so-called Boas sign, is only occasionally present. Some patients suffer from a continued auto-intoxication, with bad breath and disagreeable taste, slight elevation of temperature, and characteristic urinary disturbance. Some patients go for years suffering more or less constantly in this way without having attacks of hepatic colic and, therefore, without a diagnosis being made.

There are other instances of mild cholecystitis with cholelithiasis that are still more difficult of recognition. Some of these patients complain of gastric symptoms, which are at times extremely vague and not to be differentiated from irritative gastric symptoms, such as arise so frequently from a deranged nervous system, reflex irritation, etc. Occasionally there is complaint of severe attacks of gastralgia, not at all resembling biliary colic, of marked severity, and often regarded as a pure neuralgia. Other patients suffer from irregularity of the bowels, which condition disappears when relieved from the biliary disease. In fact the disease varies in severity of symptoms, ranging from cases having severe attacks of gall-stone colic that accompany acute cholecystitis to those cases in which the symptoms fail to attract attention, but in which gall-stones are

formed in a diseased gall-bladder and are only discovered accidentally or after death. In a large proportion of instances in which gall-stones are found post-mortem there is no history to indicate that the patient had suspected the presence of cholelithiasis.

Biliary or hepatic colic occurring at irregular intervals and which rarely can be related to a preceding typhoid infection, or other known cause, is the form of cholelithiasis most commonly met with. These attacks vary so greatly in their accompanying symptoms that it would be a difficult and tedious matter to describe them all. These differences in symptoms depend in part upon the location of the stone, in part upon the condition of the gall-bladder and surrounding structures, and in part upon the resisting power of the individual. The diagnosis is sometimes obscured by the presence of carcinoma in the vicinity; and a tumor in the head of the pancreas may so press upon the ductus choledochus, occasioning jaundice, digestive disturbances, and other symptoms, that it may be mistaken for cholelithiasis. As a rule, under the latter circumstances, the gall-bladder is distended and palpable. This group of circumstances was formerly confused with stone in the common duct accompanied by jaundice. It has been pointed out by Courvoisier, however, that when a stone in the common duct leads to obstruction, the gall-bladder is not often distended, but on the other hand contracted. There is usually, but not uniformly, complaint of pain when the stone is thus located. Jaundice is not invariable, for the reason that obstruction is not usually continuous; the stone moves, or the inflammatory edema subsides, so that there are periods in which bile-coloring matter appears in the stools. The jaundice fades, to deepen with the reappearance of the obstruction. When the stone engages and remains at the juncture of the cystic and hepatic ducts, the resulting symptoms cannot always be distinguished from those following the presence of a stone at the outlet of the choledochus. In the former condition the jaundice is apt to be persistent and the evidence of tension in the gall-bladder is relatively continuous. Often there is constant distress in the hypochondrium, varied by pain, elevated temperature, vomiting, and other symptoms of gall-bladder irritation. These cases are often very severe.

Biliary colic frequently occurs without the calculus having invaded the ducts. Occasionally the calculus engages in the opening

of the cystic duct, and through the irritation thus set up produces marked spasm of the viscus with intense pain. Colic attacks are probably not always produced from such behavior of the calculus, for the reason that sometimes we observe these attacks in cases in which the calculus is quite too large to engage in the duct. In these instances the pain is probably produced by the irritation offered by the stone to an already diseased and irritated gall-bladder, thereby producing swelling, occlusion of the duct, and spasm of the viscus. The sufferers from gall-stone disease apparently have attacks of biliary colic induced by disturbances of digestion, over-eating, and the development of a condition of toxemia, usually described by the term lithemia. It would seem to me that under these circumstances the tissues of the gall-bladder become more susceptible to irritation, just as the patients who are victims of chronic appendicitis, tonsillitis, or bronchitis may experience a reignition of the smouldering trouble through the development of the nutritive disorders just referred to. This is a point of some importance in diagnosis, because the increased acidity of the urine which occurs in the cases just referred to might mislead the observer into supposing that the pain came from irritation to the right kidney or ureter, or the group of symptoms which are sometimes experienced in those suffering from nephrotosis and which passes under the name of Dietl's crisis. There should be no great difficulty in deciding between these conditions, but I have known a difference of opinion to arise between physicians regarding them.

When in the course of cholelithiasis there develops a severe and continuous pain with swelling and rigidity in the region of the gall-bladder, with great tenderness, fever, vomiting, retching, and usually considerable tympanites, we have reason to suspect that the patient is suffering from pericholecystitis. Some recent observers go so far as to attribute all cases of biliary colic to localized peritonitis. We should not forget that in the present instance at least there is a localized peritonitis, and that it may extend sufficiently to produce the gravest results. The danger of perforation under these circumstances should always occur to one. While in fortunate cases, as the result of ulceration, a passage may be formed between the gall-bladder and the intestine, thus leading to drainage of the gall-bladder, possibly the escape of calculi (sometimes of very large size), and even ultimate cure of the case, it too often happens

that a perforation into the peritoneal cavity results from the process—following which a rapid septic peritonitis is to be expected. Many of the fatal cases of cholelithiasis follow this course.

The medical treatment of cholecystitis and cholelithiasis seems entitled to brief consideration in this place. While it is not only useless but reprehensible to delay the assistance which surgical intervention alone can bring to many patients, we are not yet in a position where it is proper to demand a cholecystotomy as soon as a diagnosis of gall-stone has been made. The majority of patients can be greatly benefited by appropriate medical treatment, and many will recover by medical treatment alone. That which seems to me of the most importance in this medical treatment is the adoption of a regimen that will prevent the appearance of a lithemic condition, a state which experience teaches is likely to induce an irritable gall-bladder and precipitate a seizure of biliary colic. In other words, the patient should not be allowed to become constipated, to have scanty and acid urine, to develop gastric derangement in which a coated tongue, disagreeable taste, flatulence, and epigastric distress are familiar symptoms. They should be made to eat simply, drink freely of water, pay special attention to the activity of the skin, exercise moderately and progressively, avoid excesses of all kinds, and assist in the elimination of waste matters by a course of alkaline saline waters, with the judicious taking of some preparation of salicylic acid. The plan selected must depend somewhat upon the resisting power of the patient, the condition of the blood, and the viscera; and the physician who understands how to avoid the recurrence of bronchitis in one subject to uricacidemia will be likely to understand the best method of preventing an irritable gall-bladder.

When the attack appears the spasms must be relieved, and for this perhaps morphin and atropin will be necessary. When the pain is not intense it may be relieved and the attack aborted by the free administration of salol, sodium salicylate, aspirin, antipyrin, and similar preparations. The patient must be kept absolutely quiet, the alimentary tract emptied carefully without producing too much intestinal peristalsis, and food must be denied. The drinking of water and sweating the patient are useful measures, and in a few instances the administration of pilocarpin has, for more than one reason, seemed to be of value. As to the use of olive oil relieving the symptoms of irritable gall-bladder, we have

a good deal of recorded experience, and for the most part it is favorable. Some advise very large, others small, doses. The plan which seems to be most serviceable is to administer a teaspoonful of oil every two hours for several days together. In case the oil leads to derangement of gastric digestion it should be abandoned. We shall undoubtedly do best in our treatment of these cases if we devote more time and thought to the conditions predisposing to the attacks.

BILIARY CIRRHOSIS OF THE LIVER, WITH AND WITHOUT CHOLELITHIASIS

A PAPER COMMUNICATED TO THE PATHOLOGICAL SOCIETY OF LONDON

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A GOOD many cases of various forms of biliary cirrhosis have been described in England, either separately or included in papers on hepatic cirrhosis in general, but without doubt the chief part of the literature on this subject is French. I need only instance the observations of Hanot, Charcot, Hayem, and the repeated publications by Gilbert and his pupils, culminating in the recent collective work by Lereboullet.¹ In England, apart from work on experimental biliary cirrhosis by Wickham Legg,² and by Vaughan Harley in conjunction with W. Barratt,³ the most important contributions are probably those contained in the various papers on diseases of the liver by H. D. Rolleston.⁴

My definition of biliary cirrhosis is: "Any cirrhosis of the liver originating from disease of the biliary ducts or obstruction to the outflow of bile." As I shall later on point out, I believe that individual tendency, or "tissue proclivity," plays a part in the development of this cirrhosis, as it does in the development of almost all pathological changes. Not every one with chronic disease in the bile-ducts develops biliary cirrhosis.

In deciding what cases of cirrhosis of the liver are to be regarded as biliary cirrhosis, too much importance must not be at-

¹ *Les Cirrhoses Biliaires*, Paris, 1902.

² On the Changes in the Liver which follow Ligature of the Bile-duct, *St. Bart's Hosp. Reports*, 1873, vol. ix, p. 161.

³ The Experimental Production of Hepatic Cirrhosis, *Journal of Pathology*, 1901, vol. vii, p. 203.

⁴ See his article on Diseases of the Liver, in the *Encyclopedia Medica*, vol. vi; on the Etiology of Cirrhosis of the Liver, in the *Quarterly Medical Journal*, July, 1899; and on Cirrhosis of the Liver in Children, in the *Clinical Journal*, September 9, 1896.

tached to the histological findings. The apparent increase of biliary canaliculi may be very well marked in ordinary cirrhosis, and may be absent in biliary cirrhosis, whilst in biliary cirrhosis the unilobular distribution of the fibrotic tissue is often not nearly so typical as one would suppose from the term monolobular (better, "unilobular"), or perilobular (better, "interlobular" or "circumlobular") cirrhosis having been occasionally used as a synonym of biliary cirrhosis. In this respect it must be remembered that Charcot and Gombault,¹ who originally introduced the term "monolobular" cirrhosis, wrote: "*Toutefois, cette régularité est loin de s'observer dans tous les cas et sur tous les points.*" Even in experimental biliary cirrhosis in animals, as that produced by Vaughan Harley and Barratt,² the distribution of the anatomical change is by no means quite regular. Professor Vaughan Harley kindly informs me that at the end of four to six months, when the cirrhosis was slight, the distribution was tolerably uniform, but that in the later cases, after twelve to sixteen months, it was markedly irregular. In biliary cirrhosis in the human subject, I believe that the changes seen by the microscope in the liver are always irregular in distribution, excepting in cases in which the disease is just commencing. The changes, however, are probably fairly uniform, and the cell-infiltration is probably confined to the interlobular spaces in cases also of ordinary cirrhosis at the commencement of the disease. Moreover, "mixed cases" may occur—that is, cases in which the hepatic cirrhosis is partly of the ordinary kind (that is, having its origin in connection with the portal blood-vessels), and only partly biliary (that is, having its origin in connection with the minute bile-vessels). It has been suggested that in late stages of biliary cirrhosis,³ owing to digestive and metabolic disturbance set up by the hepatic disease, a toxemic condition is induced in which, by the poisons carried with the blood-stream to the liver, an ordinary multilobular cirrhosis is added to the original biliary cirrhosis.

I need scarcely mention that both biliary cirrhosis and ordinary cirrhosis may be "hypertrophic" or "atrophic," though the former is more often "hypertrophic" than the latter, and is seldom really

¹ Contribution à l'Étude Anatomique de Différentes Formes de la Cirrhose du Foie, *Archives de Physiologie*, 1876, p. 469.

² Loc. cit.

³ Vide Rolleston, *Encyc. Med.*, loc. cit.

"atrophic," if the latter epithet be taken to imply that the weight of the diseased organ is actually below the normal standard. It is certainly a mistake to use the term "hypertrophic cirrhosis" as synonymous with biliary cirrhosis, or even to use the term "hypertrophic biliary cirrhosis" as synonymous with biliary cirrhosis, as is still not rarely done in England and Germany.¹ The history as well as the anatomical features must be taken into consideration in deciding which cases are to be termed biliary cirrhosis, and so separated off from the many cases of ordinary cirrhosis due to alcohol, etc.

In the present paper on biliary cirrhosis I have first taken the cases associated with cholelithiasis,² and then the cases in which no evidence of cholelithiasis or previous cholelithiasis could be detected. The illustrative cases alluded to are partly from English and partly from foreign sources.

PART I

CASES OF BILIARY CIRRHOSIS WITH CHOLELITHIASIS

CASE I.—Mrs. J. D., aged 52 years, suffered more or less from jaundice during the last seven years of her life. At one time she was very greatly relieved by operative treatment, but it is very doubtful whether at any time the jaundice absolutely cleared up, for the pruritus persisted from the commencement of her illness in 1895 to her death in 1902.

I first saw her in December, 1895. At that time she was deeply jaundiced and emaciated. The jaundice and itching had already lasted several months, and at times she had had pain in the right hypochondriac region. Considerable uniform enlargement

¹ I do not, of course, use the term "biliary cirrhosis" to include all cases of non-alcoholic and non-syphilitic cirrhosis, even when they occur in children. Non-alcoholic cirrhosis may certainly be of the ordinary, alcoholic type.

² To the cases of biliary cirrhosis with obstructive cholelithiasis should perhaps be added a few cases of biliary cirrhosis with obstruction in the large ducts from tumors and causes other than gall-stones, such as have been included by Dr. W. W. Ford in his article on Obstructive Biliary Cirrhosis, *American Journ. Med. Sciences* (January, 1901, p. 60). For the term "obstructive biliary cirrhosis" I would substitute "biliary cirrhosis from obstruction in the large ducts," since I believe that even the cases of biliary cirrhosis without obstruction in the large ducts (Hanot's disease) are to some extent examples of obstructive biliary cirrhosis, the obstruction being in the minute ducts.

of the liver was made out, but the gall-bladder could not be felt. There was a tendency to diarrhea, as there often is, both in cases of chronic hepatic and of chronic renal disease. Neither at this time nor at any time subsequently was there reason to suppose that alcohol or syphilis¹ played a part in the patient's case. Saline treatment was tried with care, but no improvement followed. The case seemed possibly one of cholelithiasis, and I thought of the advisability of an operation. Mr. Lockwood kindly took the patient into the Great Northern Hospital, and I have to thank him for allowing me to be present at the operation, and for information as to the result. At the operation, which was performed on March 7, 1896, about twelve months from the commencement of the jaundice, the liver was found to be enlarged; it was very dark, and, by its peculiar crinkled appearance when squeezed, seemed to have already undergone some fibrotic change. The gall-bladder was not distended, but contained several facettted calculi, some of which were rather friable, together with a pale greenish mucous fluid. Mr. Lockwood felt something hard at the head of the pancreas, which he thought was due to a calculus in the common bile-duct. No calculi could be felt in the cystic duct. For certain important reasons connected with the state of the patient, Mr. Lockwood determined only to do a cholecystostomy on that occasion. At first no bile came away, but two or three weeks after the operation a regular flow of bile from the fistula was established, sometimes green in color, sometimes brown, and the jaundice gradually began to clear up. The biliary fistula was allowed to close at the latter end of 1896, and the patient's general condition appeared very good. So great, indeed, was the relief afforded that the patient did not come for a second operation, which Mr. Lockwood had proposed to do for the purpose of removing the calculus from the common bile-duct. It seemed even uncertain whether this calculus was still present. However, she certainly suffered occasionally from jaundice, and it is doubtful whether the jaundice ever absolutely cleared up. She always had more or less pruritus, and xanthoma appeared in the latter part of 1896. The xanthoma was first noticed in the eyelids, but afterward the elbows and neck were affected. The urine

¹ Unless, indeed, the extreme atheromatous changes found in the aorta at the necropsy could be taken as evidence that there had been syphilis.

and feces, however, were said usually to have been natural in color. She was able to continue her work (washing clothes) till about February, 1901, when the skin became yellower and the urine darker.

When I saw her on April 25, 1901, she was moderately jaundiced, and pruritus and scratching were evidenced by a great number of scabs. Besides the yellowish tinge of icterus there was a certain amount of dusky pigmentation of the skin, such as may be noticed in most cases of very chronic jaundice; this was most obvious on the neck, forearms, and abdomen. On one thigh there was discoloration from a bruise, which was said to have arisen without any known traumatism. There were the ordinary raised circumscribed patches of xanthoma at the inner parts of the eyelids, larger raised patches about the elbows, and a few small spots about the axillæ. On each side of the neck there was a diffuse area of xanthoma, which was level with the rest of the skin; these patches had a somewhat vitiligo-like appearance, owing to the fact that they were not raised, and that the skin of the neck around them was, as I have already mentioned, somewhat abnormally pigmented. Examination of the thoracic organs showed nothing abnormal. Pulse, 78, regular. The upper border of the hepatic dulness was at the fifth rib in the right nipple line; the hard lower edge of the liver could be felt on the right close to the anterior superior iliac spine; in the middle line it was a little above the umbilicus. The spleen was likewise much enlarged; the lower border could be felt just above the left anterior superior iliac spine, and the upper margin of the dulness was at about the ninth intercostal space in the mid-axillary line. The urine was of specific gravity 1010, was clear, of neutral reaction, containing a trace of albumin,¹ free from sugar,

¹ It is perhaps only in the *most extreme degrees of jaundice* with chronic obstruction in the common bile-duct that the urine gives the *very marked* reaction for a mucinoid substance, or nucleo-albumin, to which I alluded in Trans. Path. Soc. London, 1900, vol. li, p. 176, and which is probably of bad prognostic significance. On the other hand, in all or nearly all cases of jaundice with complete obstruction to the escape of bile (even when of relatively short duration), casts can be found in the urine, if carefully searched for, though albumin be absent. These casts may contain pigment granules and pigmented cells, but have no special prognostic significance. Nothnagel (Deut. Arch. für klin. Medicin, 1874, vol. xii, p. 326) thought that in every marked case of jaundice, whatever the cause of the jaundice may be, casts appear in the urine. Cf. Dr. P. S. Wallerstein, Ueber reine Cylindrurie bei künstlich erzeugter Gallenstauung, Berliner klin. Wochenschrift, 1902, No. 14, p. 310.

and giving a moderate Gmelin's reaction for bile-pigment. In May, 1901, the patient seemed better again, and rather less jaundiced.

In August, 1901, her case was diagnosed at one of the large London hospitals as a case of malignant disease of the liver, probably commencing in the gall-bladder in connection with cholelithiasis. But the patient was able to go on with her work. At the end of March, 1902, however, the jaundice deepened again, and when I saw her in April, 1902, her condition seemed much the same as in April of the previous year, except that the jaundice was probably more marked. There was a systolic murmur over the pulmonary area of the heart. The patient was admitted to the German Hospital in July, 1902, when she seemed very cachectic, but had a fair appetite. The xanthoma had probably not diminished, as it has been said to do in some cases of chronic hepatic disease, but it had, I think, become less marked, owing to general pigmentary and degenerative changes in the skin. In July some dulness was noted at the base of the right lung, and in the latter part of the month there was a little cough and bloody sputum, but on the whole the general condition seemed again to improve a little. On the morning of August 14, however, the temperature, which since the patient's admission had never been elevated, rose suddenly to 102° F. Pulse, 100. Slight dyspnea. There was dulness at the back of the right lung, which an exploratory puncture showed to be due to a very bile-stained serous effusion in the pleural cavity. The left leg above the ankle was reddish, somewhat swollen, and tender. A painful swelling about the ankle had been first noted on the previous day (August 13). On August 16 the left leg up to the knee was bluish, and gangrene seemed to be threatening. Fever continued. Death occurred on August 17, 1902.

Necropsy.—The heart weighed 12 ounces, and showed slight hypertrophy of the left ventricle, but no valvular disease. The whole of the aorta and both common iliac arteries were extremely atheromatous, and this probably explained the threatened gangrene of one limb before death. The right pleural cavity contained bile-stained serous fluid. In one of the lungs there was what seemed to be a not quite recent infarction. The kidneys together weighed 14 ounces;¹ they seemed fairly healthy, and the capsules

¹ Thus the weight of the kidneys was somewhat above the average. I believe that in most cases of chronic hepatic disease the kidneys, if not inde-

stripped readily. The pancreas, macroscopically and microscopically, appeared normal. The spleen was large and rather soft, as it generally is in old cases of biliary cirrhosis; it weighed 36 ounces. The capsule was a little thickened in places from old perisplenitis. From microscopic examination it appeared that the increase in size of the organ was due to engorgement with blood and to a simple hyperplasia of the pulp; there was, however, a slight relative increase in the amount of fibrous tissue, especially about the Malpighian corpuscles.

The liver (weight about 76 ounces) was enlarged, greenish-yellow on section, and much cirrhotic. The surface was somewhat granular, with a few soft knobs,¹ but not nearly sufficiently puckered up to have a "hob-nail" appearance. There was no malignant disease. There was dense scar tissue at the site of the old cholecystostomy wound. The gall-bladder was contracted, containing a little pale mucus. The lumen of the cystic duct was obliterated. Bile was seen oozing out of the papilla in the duodenum. The hepatic and common bile-ducts were considerably dilated; and, freely movable in the cavity formed by their dilated channels a solitary black kidney-shaped gall-stone was found, together with bile and a few sandy particles. The gall-stone measured 12 x 9 x 5 mm., and its surface, though not polished, was not very rough. This stone

pendently diseased, are above the average in weight, and, conversely, in most cases of chronic renal disease the liver, if not independently diseased, is above the average in weight. The explanation is probably that in the former class of cases extra excretory work is thrown on the kidneys, and in the latter class extra work is thrown on the liver. In cases of chronic jaundice the continual excretion of bile must throw extra work on the kidneys, and, I believe, the kidneys of persons with chronic jaundice from any cause become both "functionally," if I may say so, and organically hypertrophied. Recently I gave one decigram of methylene-blue to two patients with very chronic jaundice, and found that their urines became free from the blue coloring matter sooner than did the urines of healthy persons who took a similar dose for purposes of control at the same hour. The methylene-blue was apparently excreted at a quicker rate by the patients, especially one of them, with chronic jaundice than by healthy persons. I am not sure whether this observation corresponds to what has been found by others; and the methylene-blue test is, it must be admitted, for many reasons unsatisfactory.

¹ Some of these little knobs were probably of the nature of regenerative hyperplasia or adenomata. Cf. H. Fraser's paper on Multiple Adenomata in Cirrhosis of the Liver (*Virchow's Arch.*, 1901, vol. clxv, p. 540) giving references to other literature on the subject. See also later foot-note.

had probably, I think, been in the choledochus since the commencement of the illness. Microscopically the liver presented the appearances of irregular multilobular cirrhosis, though possibly the distribution of the fibroid tissue was more uniform, and in some parts more approaching a true unilobular arrangement than in cases of ordinary cirrhosis. In other words, the fibroid meshwork was finer and more regular than is usual in ordinary cirrhosis. But this was more obvious by naked-eye examination of the cut surface of the organ than by microscopic examination. The liver-cells over large portions of the sections were badly preserved, and their nuclei did not stain well. The fibroid tissue, which looked swollen up, showed in parts a good deal of recent small cell infiltration. There was no obvious increase of bile canaliculi; on the contrary, it seemed as if many of the little ducts had been obliterated; typical duct-epithelium seemed to be almost absent; but these appearances may have been partly of post-mortem origin, or due to imperfect staining.¹ The liver-cells contained fine pigment granules, and apparently less fat than the cells in most cases of ordinary cirrhosis. There was likewise pigment to be seen here and there in the bands of scar tissue. Clumps of bacteria, deeply stained by Gram's method, probably a rapid cadaveric growth, were seen scattered about in the sections. I have to thank Mr. S. G. Shattock for helping me in the microscopic examination of the sections (see Figs. 1 and 2).

CASE II.—This case occurred several years ago.² The patient, Mrs. M. L., aged 55 years, suffered more or less from jaundice during the last four years of her life. There was no history of previous attacks of jaundice, nor of syphilis, nor of alcoholism (?). A friend connected the onset of the illness with troubles following her husband's death. She had had no definite biliary colic, but had had pain in the left side. There were occasional exacerbations characteristic of the chronic jaundice associated with cholelithiasis.

¹ Yet these appearances may have some significance, as they are confirmed by what has been found in my previous case (Case II) and in some other cases (*vide* Cases VI and VIII). Increase of bile canaliculi is probably a more constant phenomenon in cases of Hanot's disease (see later) than in biliary cirrhosis with cholelithiasis.

² I gave an account of it in *Brit. Med. Journ.*, April 25, 1896.

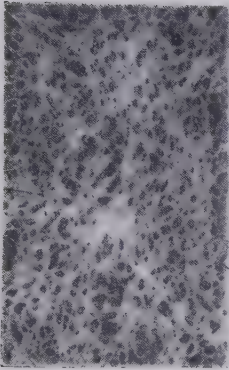


FIG. 1.—Illustrating the macroscopic appearance of a cut surface of the liver in Case I.

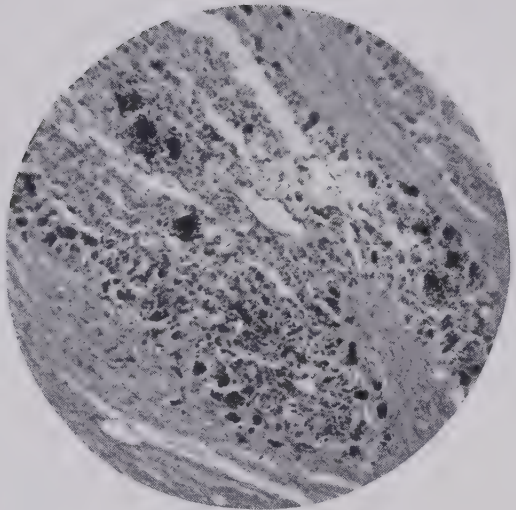


FIG. 2.—Section of the liver of Case I, showing a lobule surrounded and encroached upon by fibrous tissue. ($\times 80$.)

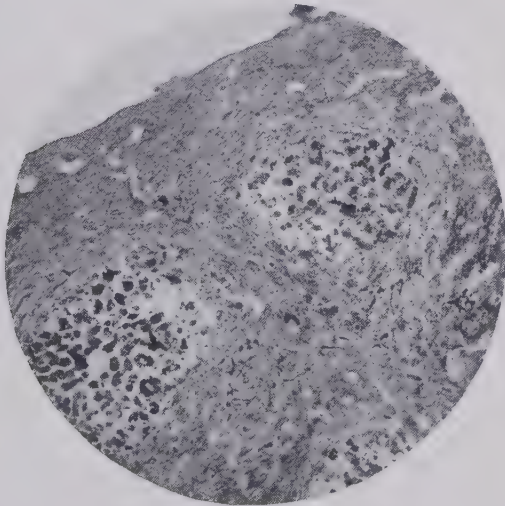


FIG. 3.—Section of the liver of Case II, showing to the left a lobule separated off by fibrous tissue. ($\times 50$.)

When I saw her first in November, 1894, the jaundice was deep; there was ordinary raised xanthoma of the eyelids, and on each side of the neck there was a diffuse area of xanthoma which, as in Case I, was level with the surrounding skin of the part. Pruritus was troublesome. The liver was hard and uniformly much enlarged, and there was no ascites. In November, 1895, the patient was readmitted in a condition of general weakness and prostration. The skin appeared darker, as if more pigment had been deposited in it. The pruritus had almost ceased. Some ascites could be made out, but there was no dilatation of veins over the front of the abdomen. The feces were colorless, often loose, and accompanied by a little blood. The urine contained much bile-pigment. There was great edema of the lower extremities toward the end. The temperature never reached 100° F. Coma gradually supervened before the patient's death (December 24, 1895).

At the *necropsy* the liver weighed 54 ounces; its substance was tough, its surface granular, and its color greenish. The gall-bladder was rather dilated and hypertrophied, and contained a thin, faintly greenish fluid; the cystic and hepatic ducts were pervious. The common bile-duct was dilated, and near its orifice, in the diverticulum of Vater, were two black gall-stones, the larger one having the size of a small cherry-stone. Fluid could, however, be squeezed out by the bile-passages into the duodenum. This case resembles Case I in many respects, but especially in the small size of the gall-stones, which at the time of death were insufficient, unless by a ball-valve action, to cause complete obstruction to the outflow of bile. The microscopic preparations of the liver (Fig. 3), which I still possess, so resemble those from Case I that I need not repeat what I said under that heading. The spleen likewise, as in Case I, was uniformly enlarged and rather soft; it weighed 20 ounces.

CASE III.—The following case has been described by Dr. C. M. Chadwick:¹ The patient was a woman, aged 36 years, who died after copious hematemesis, having for nearly six years had jaundice. The liver seems to have diminished, as possibly it did likewise in Case II, during the latter part of the disease. The xanthoma which was present is stated to have disappeared before the

¹ Brit. Med. Journ., 1895, vol. i, p. 1143.

patient's death. The *necropsy* showed general matting together of all the abdominal contents by old peritonitis and obstruction to the passage of bile by an egg-shaped gall-stone weighing 4 grams when dry. The spleen weighed 21 ounces, but is supposed to have been still larger before the final hematemesis. The liver was much cirrhotic, had a granular surface, as Dr. Chadwick informed me, and was of a decidedly green color. Through Dr. Chadwick's kindness I had the opportunity of examining sections of the liver; they resembled the preparations from Cases I and II.

CASE IV.—Dr. Humbert Mollière's case¹ was doubtless another example of the same kind, only that in his patient, a woman aged 70 years, with jaundice of over two years' duration, a large calculus seems to have completely blocked the lower part of the common bile-duct. The liver was hard, enlarged, and of a greenish color. The bile-ducts were hypertrophied and dilated, and contained a blackish powdery material.

CASE V.—S. J. Sharkey² describes the case of a young man aged 20 years, with jaundice and biliary cirrhosis, who died after an operation. There were gall-stones in the gall-bladder, but none were found in the common bile-duct. Dr. Sharkey thinks the cirrhosis in this case was an example of Hanot's disease, and not due to cholelithiasis. It must be noted, however, that the examination after death was limited to what could be discovered through the laparotomy wound. The patient's mother had apparently at one time suffered from cholelithiasis.

CASE VI.—The case of Gilbert and Fournier.³ A woman of healthy antecedents, at the age of 25 years commenced to suffer from recurrent attacks of biliary colic with fever. Jaundice, sometimes more, sometimes less, persisted from the time of the second attack until her death. On examination three years after the commencement of the illness, there were deep jaundice, pruritus, and xanthoma. The liver was enlarged and hard, its surface was smooth, and it was tender to palpation. The lower edge of the spleen could be felt five finger-breadths below the costal margin. No ascites. There was diarrhea, and the feces were sometimes colored, some-

¹ Lyon Médical, vol. xviii, p. 198.

² St. Thomas's Hospital Reports, New Series, vol. xviii, p. 245.

³ Comptes Rendus de la Soc. de Biologie, Paris, July 10, 1897, p. 692. Quoted by Lereboullet, loc. cit.

times not, according to the degree of the jaundice. Appetite good. Puncture of the liver enabled the presence of *Bacterium coli* to be recognized in that organ. No gall-stones were detected by an exploratory operation. The general condition improved, but three months later the patient suffered from hematemesis, epistaxis, hematuria, and hyperpyrexia, and she sank rapidly. At the *necropsy* the extrahepatic bile-ducts were a little dilated, and a calculus was found in the choledochus which did not completely obstruct the channel. The hepatic cirrhosis was of somewhat irregular multilobular distribution. There were no newly-formed biliary canaliculi, and a good many of the original canaliculi had apparently been obliterated.

CASE VII.—The following case was described by T. Legry:¹ The patient, a woman aged 57 years, in the clinic of Professor Cornil, at Paris, had had jaundice for twenty years. There was no evidence of alcoholism. The jaundice commenced after her sixth pregnancy, and its onset was accompanied by pains, not very severe, in the right hypochondriac and epigastric regions. Some months later on the pains were worse, but were never accompanied by vomiting. In spite of the chronic jaundice her general condition had remained fairly good until a year before admission to the hospital, when she became weaker. Six months before admission her legs and abdomen began to swell. On admission there was ascites. The feces were normally colored. The urine was free from albumin and sugar. After paracentesis and removal of nine liters of ascitic fluid, the liver could be felt hard, evenly enlarged, and reaching two inches below the costal margin. The loss of strength increased rapidly, and the patient died about two weeks after admission. At the *necropsy* the heart was found flabby, and seemed to have undergone a certain amount of fatty degeneration. There was hypostatic congestion of the lungs, and ecchymoses of the mucous membranes of the stomach, duodenum, and uterus, and of the pelvis of the kidneys. The spleen was enlarged, measuring $8 \times 4\frac{1}{4} \times 2\frac{3}{8}$ inches, and there was some perisplenitis. The liver was enlarged, cirrhotic, and its surface granular. On cutting into the organ the intrahepatic bile-ducts were seen to be dilated, and some of them

¹ Bulletins de la Société Anatomique, Paris, May 31, 1899, p. 405. Quoted by Lereboullet, loc. cit.

were blocked by concretions. The common bile-duct contained calculi, which probably did not completely obstruct it. The gall-bladder was somewhat contracted. There were enlarged lymphatic glands at the hilum of the liver, and elsewhere in the abdomen and thorax. Microscopic examination of the liver showed great fibrosis, the distribution of the fibroid tissue being in the main unilobular.

CASE VIII.—E. Tison's case.¹ The patient was a woman aged 39 years. Her illness had commenced with hepatic colic and jaundice five years previously. The jaundice had persisted from that time. She had had occasional attacks of hepatic pain, but had been able to continue her work to within a year of her death. Seven months before death she had severe attacks of hepatic pain, hematemesis, and melena. The jaundice deepened. On admission to the hospital she was feeble and emaciated and intensely jaundiced. Xanthoma was noted at the inner angles of the eyelids. There was edema of the lower extremities and slight ascites. The subcutaneous veins of the abdomen were not dilated. The liver was felt hard, and reached about five finger-breadths below the costal margin. The spleen was enlarged and tender to pressure. The feces were yellowish, never quite devoid of color. The bilious urine contained no albumin. The patient was feverish and dyspneic, and died four days after admission. At the *necropsy* the liver (weight 67½ ounces) was enlarged and hard; its surface was uneven and grayish, but the color on cutting into it was yellowish-green. The common bile-duct, the hepatic duct, and the gall-bladder were dilated and full of calculi. Some of the intrahepatic bile-ducts contained biliary sand and calculi. The spleen was enlarged and soft. The lymphatic glands at the hilum of the liver were enlarged and pigmented. The heart was flabby, and the lungs were emphysematous with hypostatic congestion. Microscopic examination of the liver showed that the cirrhosis was irregular in distribution. Some of the hepatic cells took the stain badly. Tison thought there were no newly-formed biliary canaliculi.

CASE IX.—Rabé's case.² The patient was a man aged 73 years, who died with the symptoms of atrophic cirrhosis. He never had

¹ Bulletins de la Société Anatomique, Paris, November, 1888, p. 969. Quoted by Lereboullet, loc. cit.

² Bulletins de la Société Anatomique, Paris, February, 1898, p. 170.

jaundice. There was ascites. Evidence of chronic alcoholism was forthcoming. At the *necropsy* a calculus was found in the ampulla of Vater, and there was obliterating pylephlebitis. The distribution of the hepatic cirrhosis was chiefly multilobular, but to a lesser degree also unilobular. The man seems therefore to have had ordinary cirrhosis connected with his alcoholism, and a certain amount of biliary cirrhosis connected with his cholelithiasis.

CASE X.—A. Krokiewicz's case.¹ The patient was a man aged 57 years, with jaundice, large liver, and large spleen. The illness was supposed to be of one year's duration. He died about five weeks after admission to the hospital. The *necropsy* showed dilatation of the common, hepatic, and cystic bile-ducts, and the presence of gall-stones in the gall-bladder. The orifice of the common bile-duct was stenosed by incipient carcinoma. The liver was enlarged, hard, and its parenchyma was of a greenish-brown color. Microscopically the distribution of the cirrhosis was irregular. This case can only be included here on the supposition that cholelithiasis preceded the carcinomatous stenosis of the common bile-duct.

CASE XI.—A case described by W. W. Ford.² The patient was a woman aged 28 years, with jaundice of three years' duration. She had ascites and edema of the lower extremities, and the superficial abdominal veins were dilated. Coma and death occurred about a month after admission to the hospital. At the *necropsy* the liver was found greatly enlarged, of tough consistence, and with granular surface; by microscopic examination it is said to have shown interlobular and intralobular cirrhosis, with increase of biliary canaliculi. The hepatic duct was slightly dilated, and contained a loose calculus pressing on the cystic duct at its orifice; the cystic duct was obliterated and the gall-bladder thickened.

CASE XII.—A case also described by Dr. Ford.³ The patient was a man aged 53 years, admitted to the hospital with jaundice, pruritus, and enlarged liver. His symptoms (attacks of epigastric pain and vomiting) were of over two years' duration. He died from hemorrhage after the operation of cholecystoduodenostomy, shortly after admission. No calculus was found at the operation or at the *necropsy*, but some ulceration near the orifice of the com-

¹ Wiener klin. Wochenschrift, 1898, No. 13, p. 320.

² Loc. cit., p. 68.

³ Loc. cit., p. 70.

mon bile-duct pointed to the recent passage of a calculus. The common, hepatic, and cystic bile-ducts were greatly dilated. Microscopic examination of the liver, which was enlarged, firm, and granular, showed an early stage of interlobular cirrhosis, with dilatation of the biliary ducts and deposit of bile-pigment in many of the hepatic cells.

Cases of jaundice of two to seven years' duration, or still more chronic, are to be found scattered about in the literature of the subject. Many of these almost certainly belong to the class of chronic cholelithiasis with biliary cirrhosis, and yet will not serve as illustrations, either because no post-mortem examination was recorded,¹ or because the description of the liver was omitted, or because fatal ulceration or fatal suppurative cholangitis supervened and obscured the original pathological anatomical features. Doubtless many other cases have remained unpublished; to one interesting unpublished case I shall afterward (by permission) allude.

Changes found in Biliary Cirrhosis with Cholelithiasis.—The cases of which I have given abstracts serve to illustrate the anatomical changes in biliary cirrhosis with cholelithiasis. The enlargement of the liver is fairly uniform, and though the surface of the organ may present a granular or slightly puckered appearance from contraction of the newly-formed connective tissue, and may have a few projecting nodules (possibly representing an attempt at compensatory hyperplasia² of the glandular tissue),

¹ For instance, the case reported by W. T. Mills (Brit. Med. Journ., July 6, 1901), in which a patient known to have passed gall-stones developed a large, hard liver without ascites, and died about four and a half years after the attack of cholelithiasis. One cannot help thinking that certain very chronic cases of jaundice and cholelithiasis must have had likewise some degree of biliary cirrhosis, although recovery from the jaundice was recorded. For instance, there is Van Swieten's case of a woman, 60 years of age, who had jaundice for twelve years, first at intervals, but during the last year continuously; she got rid of her jaundice after much discharge of sandy material with the feces (Commentaries of Van Swieten, English translation, 1765, vol. ix, p. 270). Then there is Murchison's case of a woman, about 40 years old, who recovered from her symptoms after more or less persistent jaundice from gall-stones during nearly six years (Murchison's Clinical Lectures on Diseases of the Liver, third edition, p. 417).

² In cirrhotic livers it is probably not always possible to sharply distinguish between multiple adenomata (that is, "hyperplasia-like tumor-formation") and nodular compensatory overgrowth of the parenchyma, as seen in

it has little or none of the coarse "hob-nail" irregularity often seen in ordinary cirrhosis. The liver is generally, but not always, much enlarged, and its color is greenish, owing probably to the long duration of the jaundice. The distribution of the newly-formed connective tissue, excepting perhaps at a few spots here and there, is not strictly "unilobular." All that can be said is that it is more uniform and more inclined to be unilobular than in cases of ordinary cirrhosis. This finer distribution in the cirrhotic process is better seen by naked-eye examination of a freshly-cut surface than by studying microscopic preparations. The hepatic parenchyma apparently contains less fat than that from a case of ordinary cirrhosis. The associated enlargement of the spleen is generally greater than in cases of ordinary cirrhosis.

I have seen nothing to make me believe that any changes occur in the bile-ducts analogous to xanthoma of the skin. I consider the theory of a xanthomatous swelling of the walls of the biliary ducts, as the cause of an obstructive jaundice and of hypertrophic cirrhosis of the liver,¹ to be exceedingly improbable. There is a good deal of evidence that all forms of xanthoma eruption (except perhaps the very slight "hereditary" or "family" cases) are associated with functional or organic disorders of the liver and abdominal viscera, whether jaundice be present or not. Even the rare form characterized as "*Xanthoma diabeticorum*" has usually occurred, not in the severest cases of diabetes, but in stout persons, often "free livers," with only slight or occasional glycosuria (in some cases even sugar has never been detected in the urine), in whom more or less chronic derangement of the abdominal viscera (liver or pancreas or both) is highly probable.

The Cause of the Cirrhosis.—I now believe that the cause of the cirrhosis in these cases is twofold—partly an obstruction to the outflow of bile from the liver, and partly a chronic inflammation of the bile-ducts.

ordinary hob-nail livers (that is, "tumor-like hyperplasia"). In either case malignant tumor-formation may supervene. The increase of bile canaliculi, when present, must likewise in part be regarded as representing a process of tumor-like hyperplasia or hyperplasia-like tumor-formation.

¹Hyde and Montgomery (*Diseases of the Skin*, sixth edition, 1901, p. 553) write: "The icterus and hypertrophy of the liver which sometimes complicate xanthoma are probably secondary and caused by the presence of the growth in the liver or in the biliary passages."

The experimental evidence in favor of obstruction to the bile flow as a possible cause of cirrhosis is very strong. Besides the English work on this subject already mentioned, I need only refer to the well-known investigations of H. Mayer¹ (1872), Charcot and Gombault² (1876), D. Gerhardt³ (1892), and D. Nasse⁴ (1894). It is quite true, as may be objected, that the existence of cholelithiasis almost implied the existence of a disordered condition of the biliary passages,⁵ but one cannot infer from this: that the cases of biliary cirrhosis following cholelithiasis are due merely to the same disorder of the bile-ducts which led to the formation of the gall-stones. If they were, one would expect biliary cirrhosis to occur more frequently with gall-stones in the gall-bladder or cystic duct, whereas in the cholelithiasis cases in which cirrhosis has developed the gall-stones have been located in the common or hepatic bile-duct. Moreover, obstruction to the outflow of bile from causes other than gall-stones⁶ suffices, if very chronic, to induce cirrhotic changes in the human subject, as it does experimentally in animals.

In regard to the way in which obstruction to the bile flow induces cirrhosis, I shall quote Vaughan Harley and Barratt,⁷ who, from experimental ligature of a single bile-duct in animals, considered the most probable explanation to be as follows:

(1) The interlobular fibrosis is attributable to the continued slight irritation set up by bile which passes through the walls of

¹ *Medicinische Jahrbücher*, Vienna, 1872, p. 133.

² *Archives de Physiologie*, 1876, second series, vol. iii, p. 272.

³ *Arch. für exp. Pathologie und Pharm.*, 1892, vol. xxx, p. 1.

⁴ *Arch. für klin. Chirurgie*, 1894, vol. xlviii, p. 885.

⁵ Naunyn (*Verhandlungen des X. Congresses f. inn. Medicin*, 1891, p. 25) believed that a morbid condition of the mucous membrane formed a necessary antecedent to the formation of calculi in the gall-bladder. This conclusion has been confirmed by the experiments of J. Mayer (*Virchow's Arch.*, 1894, vol. cxxxvi, p. 561), Mignot (*Société Anatomique*, Paris, June 24, 1898, and *Arch. Gén. de Méd.*, August, 1898), F. E. Italia (*Policlinico*, March, 1901, vol. viii, p. 153), and others, regarding the rôle of microbes (*B. coli* and other microbes if their virulence is not sufficient to cause suppuration) in the etiology of cholelithiasis. Dr. Italia gives a good bibliography of the subject.

⁶ Cf. W. W. Ford's paper on Obstructive Biliary Cirrhosis, loc. cit. Amongst other cases he quotes Benner's (1899), in which the obstruction was due to a primary adeno-carcinoma of the common bile-duct. Obstruction in large ducts is doubtless *one of the causes* of the biliary cirrhosis in cases of so-called "congenital obliteration of bile-ducts;" but to this subject I shall refer later on.

⁷ Loc. cit.

the smaller bile-ducts by osmosis, caused by the increased pressure of the bile resulting from ligature. Rupture of the smaller bile-ducts probably is not an effective factor in experimentally induced cirrhosis. (2) The dilatation of the larger bile-ducts and the marked increase of the smaller ones is, in part at any rate, directly due to the ligature, and is comparable to the extreme elongation and increase in size of the veins and venules which is seen in considerable degrees of varix of the lower extremities and in varicocele. Our observations have so far failed to afford proof of other modes of formation of the interlobular bile-ducts.¹ (3) The atrophy of the lobules is due chiefly to the irritant effects of bile which has passed out of the bile-ducts, and which acts principally, if not almost exclusively, upon the peripheral portion of the lobule. It does not appear that pressure upon the lobules caused by the newly-formed interlobular fibrous tissue is an effective factor in causing atrophy.

In neither of my own cases (Cases I and II) of biliary cirrhosis with cholelithiasis was increase of bile canaliculi obvious on microscopic examination of sections of the liver. In neither of these cases in the latter part of the disease was there persistent complete obstruction to the escape of bile by the common duct, although a small calculus lying loose in the dilated ducts may have occasionally completely occluded the orifice into the duodenum by a kind of ball-valve action. The analogy, therefore, between experimental occlusion of bile-ducts by ligature and obstruction by gall-stones is not perfect, for the experimental blocking is complete, whilst the gall-stone obstruction may be intermittent or incomplete, as it was in my two cases.

Of chronic cholangitis as a causative factor in biliary cirrhosis of the liver, I shall have to say more presently.

On the whole, in regard to its pathogeny, biliary cirrhosis, when

¹ The microscopic appearances in human cases of cirrhosis point, I think, to the canaliculi being partly original and partly newly formed by transformation of hepatic cells. D. Gerhardt's illustrations (loc. cit.) from his experimental cases point to there being a formation of new bile canaliculi by atrophy of liver-cells. I think the increase in canaliculi must partly likewise in human cases be regarded as representing a process of *tumor-like hyperplasia* or *hyperplasia-like tumor-formation*, analogous to nodular compensatory overgrowth of the liver-cells or to multiple adenomata in cirrhotic livers (Cf. previous footnote on the subject).

it is associated with cholelithiasis and dilatation of the large bile-ducts, may, I think, fitly be compared to the chronic interstitial nephritis which accompanies dilatation of the urinary passages from long-continued partial or intermittent obstruction to the outflow of urine. In both cases, moreover, an acute suppurative ascending inflammation may supervene as the final cause of death. To say that because bile passes into the duodenum chronic obstruction in the common bile-duct cannot be a cause of the hepatic cirrhosis, is like saying that because a man with urethral stricture or enlarged prostate has been able to pass urine, obstruction in the urethra cannot have been the cause of his dilated ureters and chronic interstitial nephritis.¹

I must add that a case was kindly brought to my notice by my colleague, Dr. Zum Busch (in 1898), in which a condition of obstructive cholelithiasis was found associated with jaundice of nine or ten years' duration. In spite of the long duration of the jaundice the liver had undergone decidedly less cirrhotic change than in my own cases. This may be explained either as due to relative difference in tissue proclivities, or by supposing that chronic jaundice with chronic cholangitis, but without hepatic cirrhosis, may precede the cholelithiasis and cirrhosis.

In regard to the latter supposition, Dr. Sharkey's case (VI) may, as he suggests, have been a case of Hanot's disease with cholelithiasis as a mere complication. Biliary cirrhosis, as I shall later point out, results from cholangitic changes, just as, to some extent, cholelithiasis does. In fact, in Sharkey's and some other cases the biliary cirrhosis and the cholelithiasis may both equally have owed their origin to a chronic cholangitis.

In regard to the former supposition, I believe that there is such a thing as a predisposition of the hepatic tissue (special tissue proclivity) to cirrhotic change, and that a certain amount of obstruction to the bile flow and of chronic cholangitis may fail to produce cirrhosis in some persons, which in others (more predisposed) is amply sufficient. Probably, however, the persistent presence of a calculus in the common bile-duct, with the chronic cho-

¹ May not the occasional association of pancreatic lithiasis with a fibrotic change in the whole pancreas be explained in the same way as biliary cirrhosis of the liver in cases of obstructive cholelithiasis?

langitis and intestinal and metabolic disturbance necessarily accompanying it, is sufficient in all cases ultimately to set up a condition of biliary cirrhosis.

PART II

BILIARY CIRRHOSIS WITHOUT GALL-STONES AND WITHOUT OBSTRUCTION IN THE COMMON BILE-DUCT¹

The characters of the liver in these cases are very similar to those described in the preceding section. The surface of the organ has seldom a typical coarse "hob-nail" appearance, but may be granular, or at all events not quite smooth. The cirrhotic process is generally fairly uniform, but is seldom or never strictly unilobular, as it has sometimes been supposed to be, excepting at spots here and there. There is generally increase of bile canaliculi and granules of inspissated bile-pigment are seen in the small bile-ducts and liver-cells.

The disease is mainly one of childhood and the period of growth, but may commence in later years (as in Hanot's original cases). Sometimes more than one case may occur in the same family. When it commences early the disease may lead to stunting of the child's growth, a partial arrest of development, or infantilism. It is generally associated with a tendency to bleeding from the nose, gums, etc., but these "cholemic" hemorrhages are never accompanied by the peculiar articular swellings of hemophilia. The typical form of the disease is a "hypertrophic cirrhosis with chronic jaundice" (the real "Hanot's disease," according to Hanot's original publications), but the degree of jaundice differs much in different cases, and may vary considerably in the same case from time to time (exacerbations and remissions of the disease). In some cases, apparently, jaundice may be absent for a long period at the commencement of the disease. The liver is nearly always much enlarged, but, as in other forms of cirrhosis, atrophic changes may occur, and at the post-mortem examination the organ may be found not much, if at all, increased in size and weight. The spleen is generally much enlarged, and in some cases may be excessively big early in the disease; the splenic

¹ In the present paper I shall not specially consider the cases in which a certain amount of biliary cirrhosis occurs owing to obstruction of the common or hepatic bile-duct from causes (tumors, etc.) other than gall-stones.

tumor may form one of the most striking clinical features of the case. A varying amount of pigmentation of the skin, other than icteric, is usually present, as in most cases of chronic jaundice, but in some cases this pigmentation is very striking, and may even bring the question of Addison's disease to mind. Alcohol, syphilis, and malaria play no essential parts in the etiology of the disease.

Cases of the disease have been described by Hanot,¹ Schachmann,² Gilbert and Fournier,³ Gilbert and Castaigne,⁴ Gilbert and Lereboullet;⁵ and, in Great Britain, by F. Taylor,⁶ H. R. Smith,⁷ J. Finlayson,⁸ A. W. Fox,⁹ F. J. Smith.¹⁰ Many more references are given in the recent work on biliary cirrhosis by Lereboullet,¹¹ in which he has contributed descriptions of several fresh cases. I shall here content myself with giving a short description of a case which I had the opportunity of observing, and which illustrates several important points connected with the disease.

The case¹² was that of a girl, J. S., aged 14 years, who was under my care at the German Hospital, where she died in February, 1895. She had, her father thought, been more or less jaundiced all her life, and had always been weakly and thin, though she had never had any serious acute illness. She had, I think, repeatedly had bleeding from the nose and gums. She was extremely ill developed for her age and looked very much younger than she really was. Her skin was jaundiced, and likewise much darkened from chronic pigmentation; there were two or three capillary "stigmata." The liver could be felt considerably below the costal mar-

¹ Étude sur une Forme de Cirrhose Hypertrophique du Foie avec Ictère Chronique, Thèse de Paris, 1875; and Bulletin Médical, Paris, September 27, 1893. Cf. Hanot and Schachmann's conjoint study in Archives de Physiologie, Paris, 1887, vol. ix, p. 1.

² Cirrhose Hypertrophique avec Ictère Chronique, Thèse de Paris, 1887.

³ Revue Mensuelle des Maladies de l'Enfance, 1895, vol. xiii, p. 310.

⁴ Soc. de Biologie, 1899 and 1900 (various papers).

⁵ Gazette Hebdom., Paris, April 19, 1900, p. 361. This case, like many others, is included by Lereboullet, loc. cit.

⁶ Guy's Hospital Reports, vols. lii and liv.

⁷ Trans. Clinical Soc. of London, 1898, vol. xxxi, p. 258.

⁸ Glasgow Hosp. Reports, 1899, vol. ii, p. 39.

⁹ Brit. Med. Journ., 1878, vol. ii, p. 913. Typical Hanot's disease in a boy aged 11 years whose mother was a drinker.

¹⁰ Trans. Path. Soc. London, 1890, vol. xli, p. 154.

¹¹ Op. cit.

¹² F. P. Weber, Trans. Path. Soc. London, 1895, vol. xlvi, p. 71.

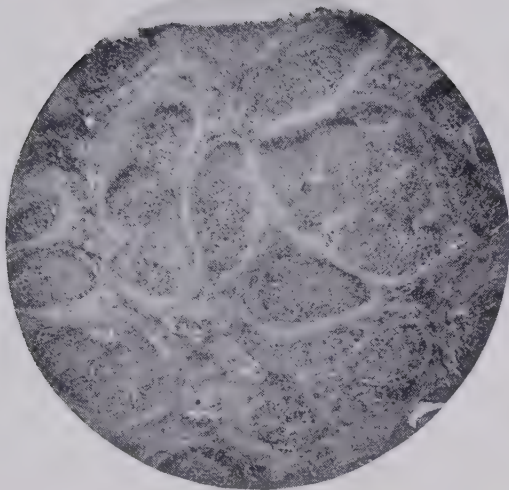


FIG. 4.—Section from a portion of the liver of J. S., showing approach to a unilobular arrangement of the cirrhotic process. ($\times 50$.)



FIG. 5.—Section from a portion of the liver of J. S.

gin, but the spleen was excessively large, reaching to below the anterior superior iliac spine. There was irregular fever, and, during the last two weeks, ascites. One sister was said to have become jaundiced at about the age of 13 years, and to have died at 19 years with symptoms somewhat resembling those of J. S. At the *necropsy* on the latter the liver was green, hard, and "hob-nailed." Perhaps I ought to have described it as having an irregular, scarcely amounting to "hob-nail," surface. It weighed only 26½ ounces. Microscopic examination of the sections showed a large amount of fibroid tissue, dividing the glandular substance into unequal compartments, and sometimes invading the lobules, entering between the individual hepatic cells (Figs. 4 and 5). There was a good deal of small cell infiltration in the scar tissue. There was not very great increase of bile canaliculi, but much green inspissated bile could be seen situated between or in the hepatic cells, which on the whole contained relatively little fat. The gall-bladder contained a moderate amount of clear, almost colorless fluid. The common bile-duct was unfortunately not examined. There was no perihepatitis. The spleen, uniformly enlarged, weighed 20½ ounces; on section its substance seemed rather firm, but otherwise normal; the microscope showed increase in fibrous tissue, and considerable deposit of pigment in some of the trabeculæ. The lymph-glands, especially those at the hilum of the liver, were somewhat enlarged and much pigmented.

Amongst the points in regard to Hanot's disease which this case illustrates, are the following: (1) In some cases of long duration the cirrhosis may be said to become almost "atrophic," instead of "hypertrophic," whilst the contraction of the newly-formed fibroid tissue and the nodules representing an attempt at compensatory hyperplasia of the gland-cells, may give the surface of the liver an almost "hob-nail" appearance, as in ordinary cirrhosis. (2) The fibrosis, though more regular than in many cases of ordinary cirrhosis, is not purely "unilobular" in distribution. (3) The growth of the patient's whole body may be stunted when the disease commences in early childhood. (4) The enlargement of the spleen, especially in children, may be so great as to constitute the most striking clinical feature of the case. (5) The case further illustrates the occasional tendency to Hanot's disease in different members of the same family. It is worth mentioning that the child's

mother was a drinker, just as the mother in Dr. A. W. Fox's case was.¹

Amongst the occasional features of the disease, which my case did not illustrate, are the clubbing of the fingers and various trophic disorders of the extremities which have been sometimes noted in patients with biliary cirrhosis and other forms of chronic hepatic disease.²

Pathogeny.—In the cases of biliary cirrhosis without, as in the cases with, cholelithiasis, I believe the cirrhosis is due to (1) chronic or subacute cholangitis, and possibly temporary attacks of acute cholangitis or acute exacerbations of chronic cholangitis;³ (2) obstruction to the outflow of bile. In these cases, however, the obstruction must be in the minute bile-ducts, and is probably due to the cholangitis. This affords an explanation for the remissions and exacerbations of the jaundice and other symptoms in the disease. If there is a condition of chronic cholangitis of the large and medium-sized ducts, one can understand that a few of the smaller ducts may be likewise more or less constantly affected, and, owing to some of the minute channels being always blocked, the persistence of a certain degree of permanent jaundice becomes intelligible. During exacerbation of the cholangitis a larger number of the minute bile-ducts will become blocked, and a temporary increase of the jaundice and other symptoms will be the natural result. This process may be compared to what takes place in chronic bronchitis. A certain amount of bronchial catarrh may exist without giving rise to much trouble, and urgent symptoms may only occur during exacerbations of the disease, when many of the small bronchial tubes become affected as well as the large ones. I do not mean to say that either the cholangitis or the bronchitis must necessarily be due solely to

¹ Loc. cit.

² *Vide* Gilbert and Lereboullet, "Le Doigt Hippocratique dans les Cirrhoses Biliaires," *Gazette Hebdom.*, January 2, 1902. These authors think that a toxemia from the cholangitic disease plays a great part in the production of the clubbed fingers and of an arthropathy which they term "biliary rheumatism," but they also think that there is an "individual element" of importance in these cases, not every one being equally liable to get clubbed fingers from the same cause.

³ Many French authors insist on an infection of the gall-ducts as the main etiological factor both in biliary cirrhosis and in chronic "simple jaundice" without cirrhosis. *Vide* Lereboullet, *op. cit.*

the local presence of microbes. One can quite well imagine that an irritation of excretory origin may cause the inflammation and the exacerbations of inflammation in either disease. In some subjects dietetic or metabolic disturbances almost certainly give rise to attacks of bronchitis or exacerbations of chronic bronchitis, and in such persons the bronchitis may be due to irritation of the epithelium from the altered quality of blood and the resulting abnormality in the bronchial secretion.

Rolleston, who has specially insisted on the probable excretory origin of the cholangitis, suggests that the latter may be due to a poison reaching the small bile-ducts by the blood, as in experimental poisoning by toluylendiamine. He aptly terms the disease commencing in the biliary radicles a "descending cholangitis," and thus distinguishes it from "ascending cholangitis"—that is, an inflammation of the bile-ducts spreading upward from the duodenum. If this supposition of an excretory and descending cholangitis be correct, as it probably is for some cases, the cholangitis and pericholangitis, which give rise to the cirrhotic changes spreading from the small bile-ducts, may be compared to the inflammation of and around the capsules of Bowman in scarlatinal nephritis (likewise doubtless an "excretory inflammation"); the resulting biliary cirrhosis may be further compared to chronic interstitial nephritis following scarlatina.¹ In both cases, moreover, one must suppose that the resulting cicatricial changes need not necessarily be progressive in character; certain clinical phenomena are thus explained (see later in regard to the occurrence of chronic jaundice without obvious changes in the liver or spleen).

Be this as it may, there can scarcely be a doubt that unwholesome substances taken in food or drink, or for some special purpose, and auto-intoxication due to abnormal conditions of the digestive organs, may be factors in the production of biliary cirrhosis, as in that of ordinary cirrhosis. It seems to me, moreover, that the question of drugs being excreted by the liver suggests the possibility of further useful drug-treatment being discovered for cases of cholangitis and biliary cirrhosis. Some drug may be discovered which,

¹ This comparison further illustrates how in a glandular organ, such as the liver or kidney, inflammation around the minute blood-vessels and inflammation around the duct-radicles are likely to accompany each other as indistinguishable parts of a common process.

during the process of its elimination from the body, exercises as salutary an effect on abnormal conditions of the bile-ducts as chlorate of potassium when taken internally does on certain abnormal conditions of the mouth and fauces; the action of urotropin in certain disorders of the urinary passages may likewise be borne in mind.

FAMILY TENDENCY TO BILIARY CIRRHOSIS (HANOT'S DISEASE)

A sister of J. S., the patient¹ to whom I have already alluded, was likewise affected. J. Dreschfeld² met with the disease in two brothers, one of whom was a drinker and the other temperate. Osler³ mentions two brothers affected with the disease. Boinet⁴ wrote of a family in which the father and two children had biliary cirrhosis, and three other children had enlarged spleens. J. Finlayson⁵ speaks of three brothers and a sister, two of whom had biliary cirrhosis, one had enlargement of the liver and spleen with icterus, and one had slight jaundice. Hasenclever⁶ has recorded an instance of three members of one family, a boy and two of his sisters, having typical biliary cirrhosis. There is therefore no doubt whatever that a family tendency to biliary cirrhosis is occasionally met with.⁷ In the same way a special proclivity to ordinary attacks

¹ Trans. Path. Soc., 1895, loc. cit.

² Medical Chronicle, April, 1896, p. 19. Quoted by Rolleston, Encyc. Med., loc. cit.

³ Principles and Practice of Medicine, fourth edition, p. 574.

⁴ Arch. Gén. de Méd., April, 1898, p. 385. Quoted by Rolleston, loc. cit.

⁵ Glasgow Hospital Reports, 1899, vol. ii, p. 39.

⁶ Berl. klin. Woch., 1898, No. 45, p. 997.

⁷ In Hindoo families about Calcutta a cirrhosis, which from histologic examination was supposed by Paltauf and Kundrat, of Vienna, to be a form of biliary cirrhosis, is common among infants and has been noted to attack several children in the same family (cf. Gibbons, The Morbid Anatomy and Pathology of the Form of Biliary Cirrhosis which occurs in Children in India, read at the Indian Medical Congress, Calcutta, 1894; also Manson, Tropical Diseases, 1898, p. 379). There have perhaps also been instances of the ordinary type of hepatic cirrhosis occurring in different members of the same family, and apart from any influence of alcohol. F. W. Jollye (Brit. Med. Journ., April 23, 1892, p. 858) speaks of a brother and sister being affected by hepatic cirrhosis, which seems to have been of the ordinary type; and though there was no history of alcohol, both the children had indulged inordinately in vinegar. R. P. Howard (Amer. Journ. Med. Sci., October, 1887, p. 350) gives the case of a girl, aged 9 years, dying of what seems to have been a biliary type of cirrhosis; whose brother died six years later, when about 10 years old, of what seems to have been the ordinary type of cirrhosis.

of catarrhal jaundice occurs in some families,¹ and in others there is a special tendency to cholelithiasis.

If one admits the existence of a diathesis which consists in a tendency to non-suppurative cholangitis (whether descending or ascending, and whether due to the local presence of microbes or not), and if one admits that this diathesis may run in families, the mutual relation of tendencies to simple attacks of catarrhal jaundice, to the more chronic "simple cholemia" (with or without actual jaundice) of French authors, to cholelithiasis, and to biliary cirrhosis, becomes evident, and an explanation is afforded for the occasional occurrence of these different types of biliary disease in different members of the same family.²

THE ENLARGEMENT OF THE SPLEEN IN BILIARY CIRRHOSIS

Various explanations have been offered for the association of enlargement of the spleen with hepatic cirrhosis. Formerly the enlargement of the spleen was generally believed to be the result of congestion from obstruction in the liver to the portal circulation. R. Oestreich³ pointed out that, in most cases, the enlarged spleen was soft, quite different to the hard spleen of passive congestion from heart disease. He considered the enlargement as mainly due to a hyperplasia of the splenic pulp, which he ascribed to irritation. Ziegler⁴ says that, though the splenic enlargement is usually regarded as due to chronic venous engorgement, the pulp is fairly soft and not so dark red as in the spleen of simple passive congestion. In a previous study⁵ I came to the conclusion that an auto-intoxication, caused by the hepatic disease, is probably the chief cause of the splenic enlargement. In biliary cirrhosis the enlargement of the spleen is generally more marked than in ordinary cirrhosis, and it is generally relatively greater in children than in adults. Gilbert

¹ H. Benedict (Deut. med. Woch., April 17, 1902) describes what seems to be a variety of this fairly common "family disposition" to jaundice—namely, a special liability, affecting two sisters, to suffer from jaundice during pregnancy.

² Cf. Lereboullet, loc. cit.

³ Virchow's Arch., 1895, vol. cxlii.

⁴ Special Pathological Anatomy, English edition by MacAlister and Cattell, from eighth German edition, p. 114.

⁵ The Cause of Splenic Enlargement in Cases of Hepatic Cirrhosis, Edinburgh Medical Journal, December, 1897.

and Lereboullet¹ think that the enlargement is due partly to passive congestion and partly to a direct infection from the liver by the blood, favored by temporary stagnation of the blood in the splenic vein. It has been suggested that both the liver disease and the splenic enlargement are due to the same cause—namely, a condition of toxemia from abnormal absorption from the alimentary canal.

In splenic anemia (including Banti's disease) it has been urged that the splenic disease causes the hepatic cirrhosis (which sometimes supervenes at a later stage of the disease) by setting up a condition of toxemia. There is, however, no reason for believing that in the cases of biliary cirrhosis, which we are now considering, the splenic condition is the cause of the cirrhosis. Even when enlargement of the spleen precedes the physical signs of the hepatic cirrhosis, it seems more probable that a condition of cholangitis, preceding the cirrhosis, gives rise, after the manner of an infectious disease, to the splenic enlargement. Many cases of chronic, sometimes congenital, jaundice with enlarged spleen, but apparently without cirrhosis of the liver, have been described under the heading "*Ictère chronique splénomégalique*," by Lereboullet² and others.

It must be remembered that in certain individuals, particularly in children, a chronic enlargement of the spleen may be caused by a temporary feverish or toxemic condition, which would not be sufficient to cause splenic enlargement in most persons. A tendency to enlargement of the spleen, and sometimes of the lymphatic tissues in general, from slight causes may occur in several members of a family. Such a special "tissue proclivity" might account for there being certain families in which several members have chronic enlargement of the spleen and suffer from persistent slight jaundice or occasional attacks of jaundice.³ It has been suggested that the

¹ *Comptes Rendus de la Soc. de Biologie, Paris, March 30, 1901, p. 375.*

² *Loc. cit.*

³ A family series of such cases was described by Dr. Claude Wilson (*Trans. Clin. Soc. London, vol. xxiii, p. 162, and vol. xxvi, p. 163*). A family series of similar cases is published by Dr. J. A. Arkwright (*Edinburgh Medical Journal, January, 1903, p. 52*), consisting of father, one son, and one daughter, in a non-malarial country, with considerably enlarged and hardened spleens, persistent slight jaundice, and occasional attacks of fever, vomiting, and temporary increase of the jaundice. In both a mother and her son, shown by Sir Thomas Barlow and Dr. H. Batty Shaw at the Clinical Society of London (May 23,

affected members of these families are examples of splenic anemia (Banti's disease), and that the hepatic symptoms are secondary to the splenic disease. Strongly against this view is what I believe to be a fact, namely, that in none of these cases has undoubted splenic anemia been known to supervene, whereas the slight enlargement of the liver noted in some of the cases, and the attacks of jaundice and fever, suggest the existence of recurrent exacerbations of cholangitis threatening to set up actual biliary cirrhosis.

From what I have said, it is evident that I am against any classification of biliary cirrhosis according to the relative size of the spleen in different cases. Thus I would not adopt the French division into cases of cirrhose biliaire "splénomégaly" or "hyper-splénomégaly," and cirrhose biliaire "microsplénique" or "asplénomégaly," though there have been exceptional cases of biliary cirrhosis without splenic enlargement.¹

CONGENITAL BILIARY CIRRHOSIS AND THE RELATION OF BILIARY CIRRHOSIS TO CONGENITAL ABNORMALITIES OF THE BILE-DUCTS

In cases generally termed "congenital obliteration of the bile-ducts," such as those collected by Dr. John Thompson² and those described by later writers, a biliary cirrhosis of the liver seems always to be present. The occasional family tendency to the disease is very remarkable. Thomson³ writes: "The parents of the patients seem generally to have been healthy people, and yet, in a considerable proportion of the cases, it is found that they have pre-

1902), there was splenic enlargement and a slight degree of persistent jaundice, but the mother, owing to the enlargement of the liver, probably had actual biliary cirrhosis. Among the cases of "Ictère chronique splénomégaly" described by Lereboullet (loc. cit., pp. 447-464) there are some family groups comparable to these. As illustrating the possible toxic or "hemo-hepatogenous" origin of exacerbations of jaundice in some cases of "Ictère chronique splénomégaly" a paper by Bettmann in the *Münchener medicinische Wochenschrift* (June 5, 1900, page 791) may be referred to. He describes the case of a merchant, aged 29 years, with a large spleen and moderate jaundice from early childhood; there were occasional exacerbations of symptoms, and there had been at least one attack of paroxysmal hemoglobinuria, the latter proving the occurrence of excessive hemolysis.

¹ Cf. Lereboullet, loc. cit., p. 418, Case 56.

² On Congenital Obliteration of the Bile-Ducts, Edinburgh, 1892.

³ Allbutt's System of Medicine, vol. iv, 1897, p. 253.

viously had one or more infants similarly affected. Instances are on record where as many as seven or even ten cases of infantile jaundice, apparently of this nature, have occurred in one family."

In regard to the pathogeny of these cases, in most instances the lumen of some portion of the bile-ducts is found completely obliterated, but in some cases no evident obstruction to the outflow of bile can be discovered. The exact site of the obliteration, when present, varies indefinitely. Thomson says that in at least one instance (Bouisson) of the disease a gall-stone was found, and this does not seem very surprising when we consider the more or less dependence of cholelithiasis on diseased conditions of the bile-ducts. Rolleston and Hayne¹ record an instance of the disease in a child who lived six months, and give references to cases not to be found in Thomson's monograph. They suggest that the disease is primarily started by poisons derived from the mother and conveyed to the liver of the fetus, and that a mixed cirrhosis and cholangitis are thus set up. This cholangitis, they say, by descending to the larger (extra-hepatic) bile-ducts induces an obliterative cholangitis analogous to obliterative appendicitis. In exceptional instances, they think, the obliterative cholangitis might be delayed and come on much later, such an event perhaps bringing Treves's case² (jaundice of sixteen years' duration from obliteration of the channel of the common duct, operated successfully in a girl of 19 years) into line with the others.

Since Rolleston and Hayne's paper, interesting communications have appeared on the same subject by J. E. Blomfield,³ G. Parker,⁴ and J. A. Arkwright.⁵ Arkwright records a series of fourteen cases of icterus neonatorum amongst the fifteen children of one mother. Death occurred in ten of the cases. The four survivors were rather weakly, but lost their jaundice after a few weeks to

¹ A Case of Congenital Hepatic Cirrhosis with Obliterative Cholangitis (Congenital Obliteration of the Bile-Ducts), *Brit. Med. Journ.*, March 30, 1901, p. 758.

² Practitioner, January, 1899. Judging from Treves's account of the progress of the case, the patient perhaps had some degree of biliary cirrhosis as well as the obstruction in the common bile-duct, for which the operation was successfully performed.

³ *Brit. Med. Journ.*, May 11, 1901, p. 1142.

⁴ *Lancet*, August 24, 1901, p. 520.

⁵ *Edinburgh Med. Journ.*, August, 1902, p. 156.

several months. The mother herself had suffered from jaundice at the age of 4 years. It is remarkable that in the survivors no hepatic disease appears to have remained. However, F. J. Smith¹ has reported a case in which an infant recovered from icterus neonatorum in a fortnight, but developed biliary cirrhosis and died at the age of 4½ years. Moreover, the case of the girl, J. S., which I recorded, may really belong to the category of congenital cholangitis and biliary cirrhosis, for she was supposed to have been more or less jaundiced all her life, and died of biliary cirrhosis at 14 years of age.

Another clinical group of cases must here be alluded to. I have to thank Dr. A. Hall for kindly telling me about a remarkable case of congenital jaundice, described by H. A. Mason,² in a girl 13 years of age. She is fairly well grown, though somewhat backward for her years, and is without physical signs of disease in any of the thoracic or abdominal organs. The liver and spleen seem not to be enlarged. The feces are said never to have been "clay-colored," but the urine gives a slight Gmelin's reaction. The child's conjunctivæ (according to the mother) were yellow when she was three days old. It seems to me, in the light of the above-mentioned cases, that Mason's case can be best explained on the supposition that from intra-uterine cholangitis or primary developmental abnormality one (or more) of the intrahepatic ducts has been blocked, or never was pervious. This would account for the persistent jaundice, and if only a small part of the whole gland is blocked no obvious enlargement of the liver or spleen need be expected; it would also account for the feces being well colored. Several cases described by French authors as "*cholémie simple*" and "*ictère chronique acholurique*"

¹ Trans. Path. Soc. London, 1890, vol. xli, p. 154.

² Quarterly Medical Journal, November, 1902, vol. xi, p. 40. At the same meeting of the Sheffield Medico-Chirurgical Society at which Mason showed his case, Dr. W. T. Cocking showed a woman, 50 years old, in whom jaundice has been present since the age of three weeks, when it first appeared. No pruritus and no xanthoma. The liver is slightly enlarged, and a dilated gall-bladder can be felt. The spleen is not obviously enlarged. The feces are little if at all paler than natural. The urine is high colored and gives a faint Gmelin's reaction. A child of the patient, born when she was 45 years old, was healthy at birth, but developed jaundice after four weeks, and died at the age of fifteen weeks. (*Vide* Quarterly Medical Journal, February, 1903, p. 104.)

are of congenital origin, and probably of the same nature as Mason's case. In these cases the serum from a blister gives a Gmelin's reaction, but the urine is said generally to be free from bilirubin, though it may give a positive reaction during exacerbations of the jaundice. The liver and spleen are not necessarily enlarged, but one or both of these organs may be somewhat enlarged, at least during exacerbations of the jaundice. Widal and Ravaut¹ recently showed a man, 29 years of age, with congenital jaundice of this kind. The general health was well maintained. The urine was free from bilirubin, but contained urobilin. The feces were well colored. The serum from a blister gave a distinct Gmelin's reaction. I have at present under my notice a case which is clinically similar to these cases, except that the jaundice seems not to be congenital, but only of four or five years' duration. The patient is a girl about 18½ years of age. Her blood-serum gives a definite slight Gmelin's reaction, and her urine, sometimes at least, also gives a faint one. Her feces are well colored. There is no obvious enlargement of the liver or spleen. The girl is fairly well grown and plump, but temporary moderate pyrexia has been observed, and there is a tendency to bleeding from the nose and gums. I suspect that this case is of the same nature as Mason's and the French cases, though it is not congenital.

After this short digression I must return to the subject of congenital biliary cirrhosis. On the whole it seems that Rolleston and Hayne's case and a number of the cases termed "congenital obliteration of the ducts" are examples of biliary cirrhosis due to a non-suppurative cholangitis,² just as the typical cases of Hanot's disease are. The peculiarity of the cases in question consists in the intra-uterine or very early onset of the disease, and intra-uterine disease may in the bile-ducts, as in other parts of the body, give rise to secondary malformation and arrest of development.

Surely, however, it is quite probable that some of the cases of "congenital obliteration of the bile-ducts" are due to primary developmental malformation. In cases of congenital valvular disease of the heart we know that it may sometimes be difficult or even

¹ Soc. Méd. des Hôpitaux, Paris, November 21, 1902.

² Doubtless, however, obstruction in the large bile-ducts, when present, is to be regarded as *one of the causes* of the biliary cirrhosis in these cases.

impossible to distinguish what is primary developmental malformation from the malformation and arrested development resulting from intra-uterine endocarditis; in the question of congenital obliteration of bile-ducts the same difficulty must arise. Needless to say, a decided family tendency to the latter condition, such as has been occasionally noted, implies the occurrence of what we may term a congenital "functional," if not organic, malformation,¹ that is, the occurrence of a "potential" disease leading afterward to organic changes. More light will doubtless be thrown on the subject by subsequent observations.

In the so-called "congenital cystic disease" of the liver a striking microscopic feature is the excess of fibrous tissue in the interlobular spaces. The distribution of this "congenital fibrosis" may be similar to that of the fibrosis in Hanot's disease, and it may therefore be suggested (for the liver as for the kidneys) that at least some cases of congenital cystic disease are the result of an attack of inflammation during intra-uterine life, from which the fetus recovered. The very sharply defined margins of the fibrous patches between the hepatic lobules constitute, however, an objection to the inflammation theory, and point to the disease being a congenital adenocystomatous growth of the biliary ducts. Moreover, congenital cystic disease of the liver has been found associated with congenital cystic disease of the kidneys and other organs, and with cleft palate and many other congenital malformations.

¹ In regard to a possible relationship between hepatic cirrhosis and other chronic diseases, on the one hand, and developmental abnormalities, on the other, cf. Hastings Gilford, *The Primary Disorders of Growth*, *Lancet*, 1900, vol. i, p. 1643.

THE VALUE OF AND INDICATIONS FOR SURGICAL INTERVENTION IN CHOLELITHIASIS

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I

THE knowledge that we have of late acquired concerning the origin and evolution of cholelithiasis is calculated to extend considerably the field of action of surgery in this disorder. Under the rule of ancient ideas, when calculi were supposed to have a humoral pathogenesis and calculous accidents a mechanical pathogenesis only, an operation was always looked upon as an exceptional affair, a make-shift, or an expedient; it was not a treatment of the disease, but it was, when this or that complication occurred, a very valuable resource, though one that was always temporary and that never protected the patient as regards the future. For lithiasis was thought to depend on some major derangement of general nutrition, or slackened nutritive process, while the normal evolution of calculi was to proceed from the gall-bladder into the intestine. When they made a long halt at one of the intermediary stages, accidents arose, accidents almost always due to biliary retention; and if the surgeon then intervened, it was principally to remove the obstacle.

This traditional view has been superseded by one more accurate; and, thanks to the results of experimentation, of more and more numerous operations, of the anatomico-pathologic examinations on the living body that they have allowed, and to the ultimate outcome of these operations, the basis has been laid of a satisfactory surgical treatment of biliary lithiasis.

This new doctrine is founded on three elements: (1) That, on the one hand, infection is at the bottom of the pathogenesis of calculi, as, on the other, it is of the accidents to which they give rise; (2) that we now understand more accurately the nature of a hepatic colic, true or false, and the evolution of calculous disease in its

different stages; and (3) that we are in possession of the ultimate results of such operations, and of analyses of recurrences.

It is indispensable first to examine these points; this is a necessary preface to the study of the indications. The problem is a complex one, and one that the physician meets oftener than the surgeon; and in solving it, in the midst of the endless variety of individual cases, ready-made formulæ are of little service.

The microbial origin of biliary calculi is demonstrated by three different proofs: the presence of microbes in the calculi has been made evident; calculi have been produced experimentally; and, finally, certain cases have been observed in man in which during an acute infectious process the formation of calculi in the gall-bladder took place under the physician's eye.

As early as 1894 the existence of microbes in the center of biliary calculi in one out of three cases found at post-mortems was demonstrated, and further research showed that this claim was well founded. Again, in January, 1897, Gilbert found in the gall-bladder of a dog inoculated with the colon bacillus a perfectly organized tiny calculus. This experiment, in order to be successful, has to be performed under special conditions; nothing but microbes of very attenuated virulence must be used, and the gall-bladder must be placed in a state of inertia sufficient to avoid the expulsion of newly-formed, soft concretions and to create a certain degree of biliary stasis, though not complete stasis. Under these conditions, true calculi, hard and stratified and composed almost entirely of cholesterin, can be produced in one case out of three.

The fact must not be lost sight of that these are experiments on dogs or guinea-pigs, and that, whatever interest they may present, the conclusions derived from them should not be applied to man save with the necessary restrictions. But other cases observed on human beings are almost as demonstrative as experiments. Calculi have been found in a boy of 14 years a few weeks after an attack of typhoid fever. In the case of a woman of 53 years, who had had typhoid fever 17 years before, and who had suffered from hepatic colics for 7 years, cholecystostomy was performed, and the cloudy liquid found in the gall-bladder contained typhoid bacilli, as also the center of one of the three calculi extracted. Another case, more striking still, was one in which 4 weeks after an attack of typhoid fever 58 small cholesterin calculi were removed from

the patient's gall-bladder, and in the purulent contents of the gall-bladder and in the calculi Eberth's bacillus was found.

It is hardly necessary to dwell on the importance of these facts, as the microbial origin of biliary lithiasis can hardly be opposed any longer; still, we must understand what is meant by this assertion and realize that the microbes act by the angiocholecystitis, or special mucous catarrh, to which they give rise. Furthermore, another element is doubtless also requisite, a certain general, constitutional predisposition; otherwise how could we explain the fact that the microbes invade the gall-bladder in one case, whereas they do not in ten others? or at any rate, if they do penetrate in the ten other cases, why do they not give rise to calculi? And how about the entire families, victims to lithiasis, which every one sees?

Consequently the infectious origin of biliary lithiasis is proved, and this point is of the greatest importance as regards treatment, for the following reasons: If we have shown that gall-stones do not depend on general and obscure humoral conditions, but on a local infectious process, or a variety of cholecystitis, the disorder becomes for the most part also a local matter, and as such accessible to direct local means. Another point. If, when the calculi are once formed, they increase and multiply, we can still be sure that they are due to a single attack of lithogenous infection. At a given moment, often very remote, microbial invasion of the gall-bladder took place, and these microbial invasions, of intestinal origin, depend on various causes, and may occur in the course of different acute disorders; at any rate, the calculous disorder comes from them, from this primordial lithogenous cholecystitis. Once more, it is a complaint of the gall-bladder and ducts, not of the bile, and lithogenous cholecystitis is comparable to many other localized infections, such as appendicitis, for instance. By removing the calculi or the gall-bladder, recovery may be complete and final. And what we shall have presently to say about recurrences, real or false, fully substantiates this way of thinking.

Finally, we find infection not only at the origin of lithiasis, but also at all the other stages of the disorder; it is the leading factor of the various complications, as well as of the prognosis of the complaint.

The bacteriologic study of the bile passages in a state of health has not yet given any final results. Experiments made on dead

bodies and on animals appeared to show that healthy bile contains no microbes; furthermore, bile withdrawn from the gall-bladder by aspiration during abdominal operations and examined was found sterile in 15 cases. But later research has shown that bile taken from animals will not give colonies on aërobic media, but will do so on anaërobic media; in addition to this the lower part of the chole-dochus has been proved to be habitually septic.

It is therefore likely that the microbes coming from the intestine are constantly trying to ascend the bile passages, and if, as a usual thing, they do not get beyond a certain point, this is not due to any specially bactericidal property of the bile, but rather to the mechanical action of the bile current which sweeps out the passages and opposes the ascent of the microbes. For this reason any obstacle to the normal flow of the bile is followed by an invasion of microbes and danger of ascending, progressive infection. This is the chief danger in a calculus halting at any stage of its migration. It can therefore be said that in lithiasis the bile passages are always threatened with infection, even when there are no characteristic septic symptoms; and bacteriologic examinations of bile made during operations on the gall-bladder and ducts are generally positive, even though the liquid is transparent and apparently normal.

Consequently, any case of lithiasis presupposes, to begin with, a causal infection, relatively mild, and which as a usual thing has long disappeared when intervention occurs; it is furthermore almost always accompanied by secondary infection, on the extent and gravity of which depend the symptoms and chance of success in operating. If the infection is limited to the gall-bladder, which is itself tightly closed by the calculous obstruction in the cystic duct, the process may seem very alarming, but really is not more than a local disturbance; if, on the other hand, a big calculus makes a prolonged stay in the larger bile passages, cholecystitis is followed by angiocholitis, and the latter, though varying in extent and gravity, is in its diffuse and suppurative form generally equivalent to a death-warrant. Infectious angiocholitis is the real danger in lithiasis, a danger that we must try to prevent, because we have no real means of curing it when once it sets in in earnest.

II

This idea of the relation of infection to lithiasis, and the many direct examinations that have now been made during operations, enable us to interpret the morbid process more intelligently and to understand more accurately its various stages and their gravity, as well as the real causes of this gravity. And this is of great help in our therapeutics and our analysis of indications.

To Professor Riedel is due the merit of having shown that the traditional understanding of the hepatic colic as a normal, almost physiologic expulsion of calculi, in a word, as a curative process, only corresponded to a limited number of cases. It usually occurs with small and numerous concretions, and in such instances there are frequent colics with slight icterus, and the calculi are found in the stools—a very important point. The colic is followed by a result, is really expulsive, and may be an agent of recovery.

It sometimes happens, however, that the concretions are not all of the same size, that one or more of them become blocked in the cystic duct, but form only a partial obstruction; the colics have still the appearance of expulsive colics, but in reality the gall-bladder no longer empties itself. Small calculi accumulate in its cavity, and it is in this form of cholelithiasis that later on the gall-bladder is found stuffed with hundreds of concretions.

But true, expulsive colic is rather exceptional; false colic, without expulsion or icterus (at any rate in the early stages without complications), is far more frequent, forming about 90 per cent. of all cases. It is closely connected with obstruction of the gall-bladder and cystic duct, and in an attack of cholecystitis in a gall-bladder that is at least partially closed.

The presence alone of calculi, even large and numerous, in a gall-bladder, with permeable cystic duct through which the bile flows in and out in a physiologic manner, is easily tolerated. Such cases are common, and the calculi are a surprise of the post-mortem room. The essential condition of such tolerance is the free communication between the gall-bladder and the choledochus, which is itself permeable all the way to the intestine.

But we must admit that, as a rule, things do not stay at that point for more than a short time. The calculi are driven toward the duct by the gall-bladder contractions, rendered more efficacious

by the liquid that has accumulated in the bladder during the attacks of false colics, and become fixed in it permanently, giving rise to one of the following types:

(1) The gall-bladder, distended with liquid, contains a single, voluminous calculus floating in the contents, while in the neck, or the cystic duct, is fastened a smaller, obturating calculus. If it is far along in the cystic duct it may escape an exploration that is not thorough, and give rise to a recurrence. We shall refer to this case later.

(2) The gall-bladder, still a dilated one, contains nothing but a transparent liquid; in the cystic duct a calculus or a series of calculi block the passage. It often happens that the obstructing calculus, instead of entering the duct, remains at the neck and forms a pocket for itself, which grows longer as the calculus increases, and which ultimately adheres to and opens into the duodenum.

(3) The calculus fits into the opening of the duct like a conical cork, adheres to it, and settles there.

(4) Finally, in inveterate cases the gall-bladder is stuffed with calculi, which arrange themselves in regular layers.

Whatever may be the mechanism, whether there be calculous obstruction of the neck or the cystic duct, or chronic inflammatory obstruction of the duct, or stricture or cicatricial obliteration—everything takes place in the gall-bladder; the calculi are imprisoned in it, and infection itself, when it exists, is limited to it. This is the *gall-bladder stage of cholelithiasis*, the least dangerous, and the one that offers the best chance for harmless and efficacious surgical treatment.

For although the migration of small or moderate sized calculi from the gall-bladder to the intestine may take place easily, and be looked upon as a species of happy release, this is no longer the case in the laborious and risky propulsion of large calculi. That the latter may be driven as far as the intestine, and that when there is only one or a few calculi, this is a possible way of recovery, cannot be denied; but we cannot be guided by exceptions, nor can we forget that the slow progression of these voluminous foreign bodies always paves the way for infection. They always stretch and leave distended the diverticulum of Vater and the choledochus; in addition, they hinder the flow of the bile and even stop it com-

pletely sometimes, and by this means create a state of affairs eminently favorable for infection. In this second or *choledochus stage of cholelithiasis* everything, therefore, is to be feared, and here is where experience has led us to a formula quite opposed to former conceptions; true, expulsive hepatic colics are relatively rare; in lithiasis the danger begins almost always with the migration of the calculi; and the practical conclusion is easy to draw—operate early, during the vesicular, or gall-bladder, stage.

III

Further evidence as to the justification of early and radical operating, a means that is no longer a treatment of the complications but of the cholelithiasis itself, is to be found in the ulterior and permanent results of such operations, that is, of complete operations.

If we can show that after complete removal the calculi do not form again and that recovery is lasting, operative treatment is manifestly the most certain of all. The common aim of all treatments by drugs or mineral waters is to get the calculi to leave the gall-bladder, or else to reduce them to silence. But the former result is rarely obtained, and could not be so without serious danger, in a great many cases; the second is incomplete and always temporary. The removal of the calculi and often of the calculous gall-bladder at the first stage is a method that is far more efficacious and thorough.

Now, true cases of relapse, of calculi reforming after proper removal, are exceptional, and all surgeons with a certain amount of experience in this branch of surgery have been struck by this fact. Thus different writers on the subject say: (1) "I do not know of a single example of true relapse, in the strict sense of the term;" (2) "I have seen no recurrence in 12 years' experience;" (3) "I have only met with a single case among 95 cases that have been followed."

This does not mean that we do not observe, more or less frequently after operations, further attacks of pain, or symptoms that appear to denote a recurrence of cholelithiasis. These apparent relapses are due to different causes, which can be divided as follows:

(a) Incomplete operations. The return of symptoms is due to a calculus, but to one that was overlooked and left behind at the

operation. Every one knows how easy it is in many instances for calculi to escape even the most careful exploration when they are buried in diverticula of the mucous membrane of the gall-bladder or cystic duct, and the expulsion of a number of concretions after cholecystostomy often demonstrates the truth of this statement. Again, there are certain conditions in which exploration and extraction are necessarily incomplete, as in an operation from the lumbar side, for instance.

(*b*) In other cases extraction has been complete, but the mucous membrane is diseased and the pain that occurs subsequently is due to the continuation of this cholecystitis; it is a case of false colics.

(*c*) Adhesions are a frequent source of secondary pain and symptoms—adhesions of the gall-bladder to the abdominal wall, omentum, or intestine, twisting or kinking of the cystic duct due to such adhesions, etc. These are noted much more frequently after cholecystostomy than after cholecystectomy, as can be readily understood; still, even after total removal of the gall-bladder the stump itself may become a source of adhesions and difficulty.

(*d*) Finally, parietal, cicatricial hernias must also be blamed, and in a considerable proportion of cases; they are usually produced by difficult and complex operations, in infected cases, which first require long incisions and are then followed by protracted drainage.

These secondary accidents, or false relapses, are usually noted after tardy operations, interventions that have become a necessity. This is an additional argument in favor of the plea that I am advancing.

IV

These long but indispensable premises will have shown the character and evolution of cholelithiasis as it should now be understood, and the value of its treatment by surgical means; they will enable us to consider the operative indications, as well as the form of operation most suitable in such instances.

A certain number of indications do not admit of discussion, and it is by them that we shall begin. It must be confessed that, even now, recourse to surgical intervention in biliary lithiasis is almost always adopted only as a last resort.

Opération is urgent in a certain number of conditions: perforation of the gall-bladder, suppurative cholecystitis, and pericholecystitis complicated by peritonitis either general already or

destined to become so. But these are unusual cases in which the source of the trouble is only detected, as a general thing, during the operation itself.

Suppurative cholecystitis alone gives indications that cannot be set aside; the high temperature, rigors, steady lancinating pain, increase of the large subhepatic tumor, painful, tense, and lifting of the abdominal wall, which itself is often red and edematous—in a word, the symptomatology of the situation—leaves no doubt as to the existence of an intracystic and pericystic abscess, which has to be operated upon.

That this is always a serious complication, with doubtful prognosis, cannot be denied; and yet the future outlook depends entirely on one single point, the condition of the bile passages, the co-existing angiocholitis. If the cystic canal is entirely closed by calculi, and if the whole trouble is limited to the gall-bladder and its immediate environment, these serious states, in spite of appearances to the contrary, are generally curable, provided the operation be done at once. As in certain forms of acute appendicitis, no time must be lost in letting the attack subside, but the pus must be found and let out at once. In some cases, even, the intervention need not be limited to drainage pure and simple, but a full and radical operation can be done, with excellent and rapid results.

But the situation is very different and the danger infinitely greater when suppurative cholecystitis is complicated with infectious angiocholitis, also suppurative; and the reason why the indication is absolute of operating at once in gall-bladder suppuration is that diffusion of the suppuration into the depths of the liver and bile passages is always to be apprehended. Still, it must be admitted that the worst forms of acute, septic angiocholecystitis are usually noted in complex cases of lithiasis at the choledochus stage, when the large bile passages have been already more or less roughly handled for some time by the migration or prolonged halt of voluminous calculi. This is the most important argument in favor of early operating. There is still some chance of success when the infection has not reached beyond the large bile passages, but if it has penetrated the liver the patient is lost and all operating is useless. Still, even in these desperate cases, Kehr is not entirely pessimistic, but writes: "I have seen patients with very marked icterus, temperature of 104° F., rigors, and very painful liver, who seemed

in such desperate straits that I was not willing to operate,—and yet they survived. I have operated on some most serious cases, in which thick and fetid bile flowed from the choledochus, and yet the patients recovered.” In such instances drainage of the hepatic duct is indispensable.

Thus, even in these advanced cases an adequate and prompt operation is the only thing to give the patient a last chance of recovery.

In another class of cases, even though the situation is not altogether so grave, an immediate decision has to be made. I mean when there is an uninterrupted succession of painful attacks that end by becoming intolerable and threaten to finish with septic angiocholecystitis. In other cases still, although the symptoms are less acute, violent, and serious, the repetition of the attacks during several weeks, with all the symptoms they occasion, ends by setting up a chronic hepatic condition, a slow and progressive illness, a species of cachexia, which can only be stopped by early intervention.

These are, then, a series of clinical dilemmas in which the action of the surgeon is not open to question and in which an intervention must be insisted on as in any other urgent situation.

The decision to be made, although less imperious, is nevertheless also evident in the following forms of cholelithiasis—in the different types of chronic calculous cholecystitis.

There are two elements then on which to base a therapeutic decision—the pain and the tumor; although often both are present in many cases, in others only one or the other manifests itself, and the clinical interpretation of the case is then less easy.

When a patient has had a number of colics, of those colics without result, without expulsion, of which I have spoken above, when he suffers constantly from the right side, when in this side beneath the edge of the ribs we find a pear-shaped tumor, with more or less regular outline, hard, tense, partaking of the liver's movements and which is clearly the gall-bladder; when, on the other hand, there is neither icterus, fever, sign of obstruction of the larger ducts nor of serious infection; when, I say, these conditions exist, an operation is indicated, barring the presence of unusual contraindications due to some other chronic complaint. An operation under such circumstances will have a good chance of success, and ought to be harmless, simple, and radical. The repetition of the crises without

result, the continuous subhepatic pain, are sufficient evidence of calculous cholecystitis, which may possibly be moderated for awhile by treatment at some mineral-water resort, but which will be certain to recur and will not be cured thereby. What occurs in such cases is simply the repetition of what we see daily in salpingitis and appendicitis; a woman of the ordinary classes of society, who has to work, does not hesitate to undergo operation, whereas in the upper classes a woman postpones her decision from day to day, until finally icterus appears, and then the prognosis is no longer the same, the lithiasis is no longer confined to the gall-bladder, the ducts are blocked, and an operation which at an earlier moment would have been simple and harmless becomes difficult, risky, and of uncertain issue.

The cystic tumor is not always as distinctly defined as mentioned above; in long-standing cases with extensive adhesions nothing is detected by palpation beneath the liver but a thick, lumpy mass with ill-defined edges in which the outline of the gall-bladder has disappeared; it is not the bladder that is felt but a mass of omentum about it. In some cases, even, there is nothing circumscribed at all, no tumor, but an indefinite induration, a sort of deep swelling that is specially noticeable on palpating from below upward. Still, in such cases it is manifest that there is something wrong deep inside beneath the liver, and that is indication enough when combined with the other symptomatology.

In other forms of the disorder it is the pain that is lacking, or which, at least, is very attenuated, and which only occurs in moderate attacks; but the digestive symptoms are very marked, denutrition increases, and the patient's general condition is bad. On local examination, either a large, distended gall-bladder is found, or an irregular tumor. The idea of cancer occurs in such cases to the surgeon's mind, and rightly so. And yet, under this rather startling clinical garb, no more is found at operation than a large gall-bladder full of liquid with a calculus in its neck, or else a thick, hard gall-bladder, covered with omentum and filled with concretions. Cancer is always to be feared in old chronic forms of cholelithiasis in patients who by their age might be suspected of this disease. Cancer is a relatively common termination of these old cases of cholecystitis; one statistics gives 43 cases out of 500 to 600, and another 34 out of 168. This is therefore a very serious

element in the question, which must be taken into account in estimating the operative indications, and which again pleads on the side of the operative treatment of cholelithiasis.

Up to the present time we have only referred to old chronic cases of cholelithiasis and to tardy operations. Each man's experience, as well as statistics, shows that the latter often succeed; but this is not the way to look at the question to appreciate the exact value of early intervention. We must take into account the large number of calculous patients who succumb to advancing biliary infection or to some incurable complication of the disorder; we must also bear well in mind the extreme gravity of lithiasis of the ducts, the much lesser gravity, and the much more simple and harmless surgical cure of gall-bladder lithiasis. In order to operate in time, we must operate at the gall-bladder stage.

There are, unquestionably, a certain number of calculous patients who recover spontaneously, often in a succession of stages, by repeated discharges of calculi. There are other calculi that remain latent, or that a special dietary and mineral-water treatment reduce periodically to a quiescent condition. Finally, large calculi can migrate directly and can be eliminated in different ways, into the intestine, for instance. We have already seen how much the risk is of infection in the first eventuality, and it is far greater still in the second; it would be difficult to conceive of a large and permanent communication between the intestine and the bile passages as a desirable termination of the disorder, not to mention the adhesions, deformities, and kinking which always follow deep fistulæ.

Therefore, if it is evident that the bladder contains calculi, and if these calculi cause painful symptoms, false colics without expulsion, nothing is to be gained by permitting the attack to occur over and over again; the only result obtained from such a line of action will be the possibility of secondary obstruction of the large bile passages.

Such is what may be called really early intervention; no doubt it will be difficult to get this idea accepted, both by patients and by physicians, but it will be useful, none the less, to define clearly what it is and to lay down plainly its rational indications.

V

The point that doubles the utility of really early interventions is that they enable us to apply a thorough surgical treatment, and to put the calculous patient in the best possible condition for permanent recovery. The facts of the case are that at the present time removal of the calculous gall-bladder, cholecystectomy, is more and more becoming the operation preferred. Recent ideas as to the pathogenesis of calculi in primitive lithogenous cholecystitis, are all in its favor; it insures prompt recovery, and prevents persistent fistulæ, adhesions, and parietal hernias, and we have shown above what the importance is of these factors in false recurrences.

Finally, experience, the best of all arguments, shows the excellent and lasting results of cases of cholecystectomy. It is they that have led surgeons gradually to resort to the total and immediate removal of the gall-bladder, and the results of their increasing boldness have almost always been satisfactory. On my part, I have patients who have undergone cholecystectomy seven, six, and five years ago, and who, after very simple recoveries, have remained free since that time from all local trouble. The ultimate results of cholecystostomy are not always so good.

The tendency to which I have referred is very general. At the Medical Congress of 1900, Michaux said that he regretted that cholecystectomy was not more frequently performed, as he thought that it gave better results than cholecystostomy without exposing the patients to unending fistulæ, and as it protected the patients from recurrences. In 45 operations on the biliary ducts he had performed cholecystectomy 32 times, with 28 recoveries and 4 deaths, and after following his patients for a long time, ten and eleven years for the first ones, he was convinced of the excellent lasting results given by this operation. More recently Milhiet also has been defending cholecystectomy, and has collected 112 cases with 14 deaths, of which 5 only were due to the operation itself, a death-rate of 4.46 per cent.

Kehr, again, resorts more and more to total removal of the gall-bladder, which he often combines, when there is lithiasis of the larger ducts, with drainage of the hepatic duct. He now considers drainage of the hepatic duct, combined with cholecystectomy, as the normal method of surgically treating chronic, relapsing chole-

lithiasis. Riedel, who has been one of the principal promoters of cholecystostomy, even advises at present the removal of the gall-bladder in mild cases when it contains only serous liquid and thickened bile, with a calculus in the neck or in the cystic duct.

It is manifest that cholecystectomy presupposes two indisputable conditions: (1) a free choledochus, and (2) infection of the bile passages must not be too advanced.

The first cannot be disputed; to remove the gall-bladder and the cystic duct when the permeability of the main biliary duct is not assured, would be an absurdity, and an error that would often be fatal. On the other hand, the fact cannot be denied that, once the gall-bladder is removed, any occlusion of the choledochus that might occur later on would be very difficult and risky to cure. Cholecystenterostomy would no longer be possible, and connecting the choledochus or hepatic duct directly with the intestine is not a harmless or easy operation.

This is all true, but we suppose that the decision to remove the gall-bladder will not be taken until the permeability of the choledochus has been verified by catheter and palpation. This point understood, we may say that ulterior occlusion of the choledochus is in reality so unusual an occurrence that it need hardly be taken into consideration.

The second condition, the degree of the infection of the bile ducts, is of the greatest importance, and this it is that must guide the surgeon in his decision. For we know that drainage is our best means of defence against biliary infection, and every one is cognizant of the excellent results given by cholecystostomy in angio-cholecystitis.

Now the bile ducts must in practice always be looked on as infected. Experience has shown long ago that such is generally the case. Are we to infer from this, as was at first thought, that drainage is always necessary? This can hardly be maintained. If the larger ducts are free, why not admit that drainage by the natural passages can be efficacious? Is not this the normal means of defence of the bile ducts against ascending intestinal infection? But however this may be, facts are facts, and the nowadays numerous examples of complete and lasting recovery after cholecystectomy show that permanent flushing of the bile ducts by the bile, if nothing prevents its natural flow, is often quite enough to disinfect them.

This is, after all, only a question of degree; and clinical reactions, on the one hand, and direct examination during operation, on the other, will enable a decision to be made. If, therefore, the larger ducts are free, and if clear or thickened bile or serous liquid is found in the gall-bladder, although the contents must always be looked on as septic, there is nothing to prevent a radical operation. The case is, however, quite different when there are serious, acute symptoms, angiocholecystitis, and when the bladder contents are thick, purulent, or sanious.

In my opinion, the problem presents itself at the present time in these terms: when an operation is done for acute, pyretic symptoms, when the bile is thick and purulent, and when the cystic duct is open or incompletely obstructed, cholecystostomy is still indicated; at any rate, if the gall-bladder is removed, drainage of the hepatic duct should be instituted. In old, chronic cases, in which the acute process is long finished, in recent cases of hydrops vesicularis, and even in calculous cholecystitis with purulent contents when the cystic duct is closed and the scene is confined to the gall-bladder, it will be best at once to perform cholecystectomy.

Without wishing to lay stress on the technic of the operation, which is now well known, a few remarks on the subject may still be of interest.

To begin with, the first part of the operation—no matter what decision is ultimately adopted, and for the purpose precisely of coming to a decision—should consist in as complete an exploration as possible of all the bile ducts. We cannot say in advance that we will do this or that operation; we must first *see* how matters stand, and after having seen, while in the abdominal cavity and operating, a decision can be taken.

Evacuation of the gall-bladder—freed from adhesions and the omentum that is so often around it—is generally indispensable, in order to get room and better to carry out the deeper palpation. The process recommended by Kehr will be of great assistance: the physician with his index finger should follow the cystic duct from below upward and from without inward; the gall-bladder, closed with a forceps and stretched outward, enables the canal to be easily found. From there pass along to the choledochus, entering Winslow's foramen if it is not obstructed by adhesions; the finger should go to the further end of the choledochus, and, without going into

minutè detail, the general rule can be laid down that as much room as possible must be obtained if a really useful exploration is to be effected.

Kehr advises, before proceeding to decorticate, to place a forceps as far along as possible on the cystic duct to prevent any propulsion of calculi, or septic liquid, into the choledochus. The step that is sometimes difficult in cholecystectomy is to free the upper surface of the gall-bladder from the liver. It must be split or peeled off; this is the only means to prevent tears in the hepatic substance, with blood oozing which is often very difficult to check.

Tie the cystic duct with catgut, not with silk, which may be the origin of secondary concretions; a double ligature is a good precaution. Still, even this does not prevent bile-oozing which occurs from time to time, though in only a temporary manner, and whose origin is furthermore a disputed point. For these reasons drainage is almost always a good and prudent practice, but drainage that admits of complete and solid uniting of the greater part of the incision.

As for cholecystostomy, it will probably become more and more an operation of necessity; excellent, no doubt, in the circumstances already referred to, or else a temporary step, destined at a later moment to be completed by a cholecystectomy.

Except in certain cases, in which it may be considered to be an operation of extreme urgency where nothing more is possible than opening and draining the gall-bladder, it will always comprise the complete removal of all calculi from the bladder, neck, and cystic duct. To accomplish this, the method of gradually opening the neck and duct on the lower side, combined with retropulsion of calculi with the finger which brings them from the choledochus toward the gall-bladder, is a means that is now in general use and that gives the greatest service.

In some cases it is impossible to unite the gall-bladder with the skin, as the former is buried, retracted, sclerous, and fastened on all sides by adhesions. It is then that Poppert's hermetic drainage may be very useful; when the gall-bladder has been emptied as well as possible, a drain is inserted into it and the flaps of its walls are gathered around it by a thread—like a purse-string. A few stitches on the omentum close the region and form a sort of tunnel going from the stump to the skin. In other cases the same result

can be obtained more simply by placing a drain in the gall-bladder and some aseptic gauze in the surrounding area.

Our purpose is not to enter into the details of operations necessitated by gall-bladder lithiasis complicated by lithiasis of the larger ducts. Our aim at the present day should be to try to lessen, as far as possible, the necessity for this complex surgery of the larger ducts by operating in cholelithiasis as early as possible, at the vesicular, or gall-bladder, stage, and by making this early operation one that is simple, safe, radical, and definitely curative.

THE SURGICAL AND POST-OPERATIVE TREATMENT OF CHRONIC GALL-STONE DISEASE

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THE symptoms and diagnosis of acute affections of the gall-bladder and biliary tract are well defined and easily recognized in the majority of cases. It is true that acute cholecystitis is frequently confounded with appendicitis, and that an attack of gall-stone colic may resemble that of acute pancreatitis; but the need of operation in all of these conditions is so evident to nearly every practitioner of medicine, that such cases soon fall into the hands of the surgeon.

When we approach the chronic forms of gall-stone disease, however, and endeavor to formulate indications for treatment, difficulty is encountered. The first obstacle to be met and overcome is that summed up in the too common term, "chronic dyspepsia." Turning to the pathology of the disease in question, this can be more clearly understood.

As in acute appendicitis or acute salpingitis the peritoneal tissues adjacent to the seat of lesion become involved and at an interval operation a mass of adhesions is encountered, so also in cholecystitis a certain degree of pericholecystitis is found. This suffices to cause adhesions between the omentum, colon, duodenum, stomach, and biliary tract. The dragging effect of these adhesions, the hindrance to the peristaltic movements of the intestinal canal, the obstruction to the free action of the pylorus and the consequent dilatation or ptosis of the stomach are all of sufficient moment to cause symptoms referable to the gastro-intestinal canal.

The majority of mankind are subject, at some portion of their lives, to more or less severe attacks of abdominal pain. The ever-ready hypodermic syringe or even a dose of castor oil or other purgative usually affords relief and recovery is soon established. This attack is sometimes remembered, but often forgotten. The slow contraction of adhesions to the stomach hampers its contractile

force, stomach bitters and various preparations of *nux vomica* long continued induce atrophy of the secreting cells, and chronic gastritis or gastrectasis becomes a real and distressingly evident condition.

An atrophic gastritis or a dilated stomach is by no means caused by pericholecystitis only, but the frequency with which the only apparent symptoms observed in chronic gall-stone disease are referred to the gastro-intestinal tract is the basis of these remarks.

Chronic gastric ulcer may strongly simulate pericholecystitis and needs to be carefully diagnosticated. But even here the surgical operation of gastro-enterostomy offers more hope of permanent cure than purely medical measures.

The subsidence of an attack of severe biliary colic and the passage of gall-stones in the stools may be the cause for congratulation at the happy result of such illness; but it is doubtful whether any but the smaller stones can pass through the narrow duodenal orifice of the common duct. It therefore follows that the passage of a large stone in the stools means that a fistulous communication has taken place between the biliary tract and a neighboring viscus, usually the duodenum, colon, or stomach. This, again, means extensive adhesions, and sooner or later some form of persistent gastro-intestinal irritation.

The second obstacle to a diagnosis of chronic gall-stone disease is encountered when jaundice has never been experienced by the patient. It is not the least exaggeration to state that in 80 per cent. of the cases icterus is never experienced. No further emphasis need be made.

In certain other cases the initial gall-stone seizure may subside, leaving behind a chronic pancreatitis or cirrhosis of the liver, while the presence of muddy, stagnant, slightly infectious bile in the gall-bladder is provocative of many fatally terminating liver infections.

Cirrhosis of the liver occurs in gall-stone disease from one of two causes: The obstruction in the common duct allows a deleterious action of retained bile upon the liver cells, or the infection from the duct or gall-bladder reaches the liver by extension, the resulting angiocholitis frequently producing the cirrhosis.

Pancreatitis, either acute or chronic, accompanies gall-stone disease in many instances, and for the reason that in both diseases the same factors operate. Infection and obstruction of the excretory

ducts of the pancreas and biliary tracts are responsible for the lesions of those organs.

The common duct can never be considered in any light other than that of an infected tube liable at any time to prove a source of deadly menace to the organism; with an increase in virulence of the bacterial contents of the duct, a wave of infection may spread rapidly upward with a cholangitis, cholecystitis, and angiocholitis occurring in succession. But in most cases the infection is milder in type and reaches its greatest activity in the gall-bladder. It can be emphatically stated that gall-stones are always the result of precipitated salts and tissue débris following in the wake of bacterial infection, mild or severe in degree. Furthermore, the complications of chronic gall-stone disease, adhesions, ulceration, fistulæ, liver and pancreatic disease, etc., are also due to infection.

With these few remarks made with the intent of emphasizing the importance of the early recognition of chronic gall-stone disease, the subject proper of this paper can be approached.

The treatment of chronic gall-stone disease, its complications and sequels can only be surgical, if any good is to be accomplished. Gall-stones are formed, to repeat, through the aid of infection and therefore the disease is local and requires local treatment, that is, operation, and not solvents or cholagogues to relieve a condition resulting from faulty metabolism.

The success of operation for any one of the conditions mentioned in this paper depends upon strict asepsis, despatch in execution, mechanical dexterity, and an intimate knowledge of the anatomy of the parts involved. The preparation and protection of the field of operation within the abdomen, thorough hemostasis, adequate drainage, and a perfect peritoneal toilet are also necessary. The abdomen should be opened through the right rectus muscle and over the gall-bladder region, and a tour of inspection made, as it were, to decipher the pathologic conditions so far as can be done by superficial inspection aided by palpation. By such examination the presence of adhesions, either in the shape of bands or gluing of the great omentum to the lower border of the under surface of the liver, to the free border of the gastrohepatic or lesser omentum, to the hepatic flexure of the colon, the gall-bladder, duodenum, or stomach, will be determined. In the presence of such adhesions careful dissection must be made in order to expose the gall-bladder, its ducts, and

the common duct, the two latter occupying the right free border of the gastrohepatic or lesser omentum. To make this exposure the surgeon must be familiar with the signboards and signals, the interpretation of which will either lead him safely to his destination, or may cause destruction of life, depending upon the mode of interpretation.

The anatomic landmarks, be they normal or pathologic, must be properly discerned to insure a safe outcome to the operative procedure. The adhesions or adherent structures are freed after properly protecting the abdominal cavity against infection. Such protection is made through the medium of gauze pads and marine sponges properly placed. These sponges are used in two sizes; "large flat" and "small square" will perhaps best explain their appearance, and they are preferred for the reason that escaping bile is more rapidly absorbed by them. Their preparation for use in operations should be entrusted only to a careful and competent assistant. The opened abdomen is held widely apart by retractors and the intestines and great omentum are covered with several of the usual gauze pads and over these two or more flat sponges. The space beneath the right lobe of the liver is filled in with several of the small sponges, hepatopexy being unnecessary. A small sponge is pushed under the right free border of the gastrohepatic omentum if the adhesions are not so extensive as to shut off this space. Finally, a sponge is placed over the lesser omentum and sometimes a piece of moist gauze is made to encircle the anterior surface of the liver. This elaborate preparation is necessary because bile can never be regarded as sterile, and in the presence of gall-stones must always be considered as infectious. The writer fears but little the dissemination of sepsis under these circumstances, having so much confidence in the operative technic he practises.

After preparation of the field of operation, separation of the adhesions and adherent viscera, which would otherwise prevent the complete exposure of the gall-bladder (so essential in these operations), is performed with the fingers, scalpel, and scissors, the surgeon being careful to guard scrupulously against any hemorrhage.

In difficult cases of gall-bladder surgery I consume much more time in exposing the actual site of lesion than I do in the removal of the lesion. I am in the habit of saying to my classes, as I would say to any young man starting out in the world, Start right,—if a

young man does not start right his ending will too often correspond with his beginning. If you do not start right in an operation it is exceptional for you to end right. The practice of tearing, dragging, and clawing away structures with the sole aim of reaching the goal, the actual lesion, without considering the means by which it is reached, cannot be other than cause for disaster.

With but rare exceptions patients should not die on the operating table during these operations, nor should they die from post-operative peritonitis. The site of the lesion or lesions having been exposed, some of the smaller sponges are rearranged or new ones placed in position in order to further avoid any possibility of contamination when the gall-bladder or the common or the cystic duct is opened.

The proper placing of the large flat sponges will enable the assistant to retract the parts and thus do away with instruments made for this purpose and which when used are too often in the way. The further operative procedure will depend upon the character of the lesion. It is difficult to formulate exact indications for each procedure and much will be learned by experience. Cholecystectomy has become the operation of choice with many surgeons, whenever practicable, and in all lesions of the gall-bladder this operation may be said to be indicated, provided the operator is sure of two facts: (1) the common duct must be patent, and (2) the liver ducts must be free from infection. In other words, in cases of hydrops with or without a stone in the cystic duct, or in long standing cases of calculous cholecystitis without liver infection, cholecystectomy may be performed without draining the hepatic duct. Both the finger externally and the probe within the duct should with certainty prove the patency of the common duct. One word of caution should be given in regard to performing cholecystectomy. If ulceration, stricture, or adhesions threaten the future patency of the common duct, the gall-bladder should not be removed, as a subsequent cholecystenterostomy is of course impossible, and the operator is forced to make an external fistula or anastomose the duct to the bowel. In the absence of the gall-bladder, the fistula requires extensive gauze packing, and choledochoduodenostomy is very difficult to perform safely.

In this operation, after the protecting gauze and sponges have

been arranged, the gall-bladder, if distended with fluid, is carefully aspirated, and when emptied the opening made by the aspirating needle is enlarged and the interior of the gall-bladder examined. Any calculi present may be removed, but in the presence of active infection it is better to make no attempt at the removal of the stones separately; the opening should be clamped with hemostatic forceps and the entire gall-bladder with its contents should be excised.

One should remember that the gall-bladder and the cystic duct hold the same relation to the common duct as do the cecum and the anterior longitudinal muscular band to the appendix. Traction upon the former makes evident the common duct in the right free border of the gastrohepatic omentum, as does traction upon the cecum and the anterior longitudinal muscular band make evident the base of the appendix.

When the gall-bladder can be dissected free from the liver, commencing the dissection at the fundus and carrying it toward the cystic duct, and when the integrity of the gall-bladder will permit of traction, the outline of the cystic duct, the common duct, and the cystic artery is very beautifully demonstrated and made easy to deal with. When feasible, we should allow that portion of the serous coat of the gall-bladder adherent to the under surface of the liver to remain intact, in this wise preventing oozing from the torn liver substance, which is very difficult to control with sutures. The cystic duct and the cystic artery are carefully tied so that there will not be leakage from the former or hemorrhage from the latter. It is better to tie the cystic duct with catgut.

When the infection from the diseased gall-bladder seems to have invaded the liver the operator may consider it best to establish hepatic drainage. This is obtained by the introduction of a tube into the part of the cystic duct still remaining, granting that the latter is healthy; if not, and hepatic drainage is believed to be essential, the cystic duct is tied off flush at its junction with the hepatic duct and the upper portion of the common duct opened and a drainage tube, directed upward, introduced therein.

The operative technic for chronic catarrh of the gall-bladder with swollen ducts will, in the majority of instances, consist simply of drainage, cholecystostomy. In introducing drainage under these circumstances I first carry a purse-string suture through the serous, muscular, and submucous coats of the gall-bladder, about one inch

from the fundus, then aspirate and open the gall-bladder, and introduce a solid rubber drainage tube, and fix it to the margin of the wound in the gall-bladder with a catgut suture. With a pair of tissue forceps the drainage tube with the surrounding gall-bladder wall on the distal side of the purse-string suture is grasped, the tube pushed into the gall-bladder, and this portion of the gall-bladder invaginated. The purse-string suture is then tied, care being taken in tying the suture not to collapse the tube. Two small pieces of gauze are then introduced alongside of the tube, one in front and one behind, and the peritoneal toilet is made.

If there is evidence of the catarrhal condition having invaded the hepatic ducts and it cannot be definitely ascertained that the cystic duct is normally patulous, hepatic drainage, by introducing a tube into the upper portion of the common duct, is practised.

In the treatment of chronic pancreatitis one of three operative procedures is practised: External drainage of the gall-bladder; internal drainage of the gall-bladder by anastomosing it to either the duodenum, a loop of the jejunum, or the hepatic flexure of the colon (never anastomosing it to the stomach); and, drainage of the common or hepatic duct.

Adhesions to the peritoneum, omentum, and neighboring viscera, with their attendant evils, are separated, unless so organized that to separate them would be to endanger the viscera to which they are attached. They may be divided between hemostatic forceps, any bleeding points being of course secured. When adhesions are extensive and attached to the stomach, particularly the pylorus, and there is resulting traction on the pylorus and dilatation of the stomach, it may be more propitious not to make an attempt to deal with adhesions, but at once to do a posterior gastro-enterostomy. If the pyloric orifice is also the site of an infiltration and thereby contracted, in a certain percentage of cases, pyloroplasty is performed in connection with posterior gastro-enterostomy.

In dealing with fistulæ between the biliary tract and the various organs, fixed and fast rules cannot be laid down, as the surgeon must use his judgment, taking advantage of his experience in dealing with like cases in the past. In some cases I separate the connection between the organs and close the openings separately, while in others I allow them to remain intact, especially when it is possible

to deal with the actual lesion without forcing a separation to gain access to the site of lesion.

In obstruction of the common duct by stone the duct should be opened and drained, with the exception of the cases in which the stone occupies the sinus of Vater and it cannot be crushed between the fingers or dislodged into the common duct—in which case a duodenocholedochotomy is the operation of choice.

In stricture of the common duct the result of chronic catarrh or ulceration from the passage of a stone, the stricture should be cut in the long axis of the duct, if possible, and a T-shaped drainage tube introduced,—one end being engaged in the common duct to the proximal side of the stricture, the other end in the common duct to the distal side. The tube should be allowed to remain at least two weeks, the rationale of this procedure being the same as the introduction of a catheter after division of a stricture of the urethra. In another class of cases one should do an anastomosis of the gall-bladder to the duodenum, small or large bowel, to guard against recurrence of the trouble in the event that the stricture of the duct does not recover itself and that there is recontraction of the stricture.

In dealing with carcinoma of the bile ducts and gall-bladder it should be readily understood that early operation offers the only hope in all but a small percentage of cases. Small growths of the common duct can be removed and the duct treated as in the case of a stricture of the duct, with or without anastomosis of the gall-bladder. In carcinoma confined to the gall-bladder, removal of the gall-bladder is indicated. In carcinoma involving the liver, if circumscribed and not involving much area, excision may be done; if the growth has extended to any degree it is better to terminate the operation at once.

Persistent fistulæ from an opening in the common duct after drainage, and with or without cholecystectomy, furnish the indication that the common duct is obstructed. This obstruction may be due to a stone overlooked at operation, to stricture consequent upon ulceration, or to the constricting effect of adhesions. The cause of the obstruction must be treated; and the high mortality from a second operation upon the duct should point a lesson toward earlier operative interference in gall-stone disease. To wait until the stones have been forced into the duct is to invite a catastrophe.

There are many details to be observed in gall-bladder operations

which depend so much on the varying conditions met with at each operation that a "word description" is impossible. The amount of gauze used for drainage in association with the rubber tube, should be the minimum, and yet sufficient to take up any oozing and to promote the formation of adhesions required for the external fistula after the hepatic drainage tube has been removed. This fistula persists until the common duct becomes clear, when healing and closure are rapid and uneventful.

When cholecystostomy has been performed and a fistula persists, its repair is not difficult, as a rule. The gall-bladder may be dissected free from the peritoneum and the fistula closed by inverting the wall of the gall-bladder, using a continuous Lembert suture, with the understanding, of course, that the cystic duct is patulous. A fistula discharging mucus only, sometimes follows cholecystostomy and means obstruction of the cystic duct. Cholecystectomy or cholecystenterostomy will be required. A persistent gall-bladder-biliary fistula will call for careful examination of the common duct for obstruction which, if present, must be removed, whereupon the fistula in the gall-bladder can be closed, and the gall-bladder removed or anastomosed to the duodenum, colon, or small bowel.

POST-OPERATIVE TREATMENT

The first precaution to be taken in the care of gall-bladder cases after operation is the prevention of pneumonia. These patients are peculiarly liable to affections of the respiratory tract, such as, pneumonia, edema, and bronchitis in its various forms. The patient after operation, therefore, should at once be carefully wrapped in extra woolen blankets, and, if at all necessary, surrounded with hot-water bottles. In the removal to the recovery room great care should be taken to avoid draughts. Wrapped in the blankets the patient is put to bed; external heat in the form of hot-water bags properly placed is supplied; and the nurses in charge are especially cautioned to keep all windows closed and to exclude all currents of air.

If a rubber drainage tube has been employed the free end is at once placed in a suitable receptacle, the simplest being a wide-necked bottle. Into the bottle is placed a measured amount of some anti-septic fluid, such as a 5 per cent. solution of carbolic acid and glycerin in water; into this liquid the tube must dip, because,

especially with a tube in the hepatic duct, infection could be introduced directly into the biliary passages.

The condition of the patient now demands attention. At the German Hospital in this class of cases fortunately we have never had to deal with true surgical shock. If such a condition were to arise we should treat it on general principles.

In our general management we have no special routine, and we are guided entirely by the conditions met with. For general depression and sweating we prescribe atropin 0.0003 gram ($\frac{1}{200}$ grain) and strychnin 0.002 gram ($\frac{1}{30}$ grain) hypodermically. If this is insufficient normal saline solution 250 c.c. with 30 c.c. of whiskey is given at a temperature of 115° F. by the bowel and repeated every hour or two until reaction has set in. If the condition of the patient demands further supportive treatment we continue the use of strychnin at three-hour intervals as long as necessary. Along with the strychnin it is our custom to use saline solution and whiskey by the bowel every three hours and to continue them for about six hours or longer. This has always proved to be productive of most excellent results, as patients recover their normal tone very rapidly and peristalsis appears undoubtedly to be stimulated, to say nothing of the marked improvement of a weak and rapid pulse. We have never noted any amelioration of thirst. In a few cases a vasomotor stimulant is especially indicated, and ten minims of the solution of adrenalin chlorid (1 to 10,000) in a hypodermic-syringeful of normal salt solution has proved to be very satisfactory.

By these means, after six to eight hours, we usually find our patient in a very good general condition, and then we govern our treatment accordingly, discontinuing whatever medication has accomplished its object, it being a mistake to overstimulate.

From eight to twelve hours after operation, if there is no nausea or vomiting, we allow our patients ice chips at intervals of half an hour, and cautiously increase the amount slowly, with shorter intervals, if the stomach does not rebel. Ofttimes 5 to 10 c.c. of hot water (given in a horn spoon) is better, as it seems to be more effective in allaying the thirst, and besides it does not irritate the tongue. If all is well, the amount of water is gradually increased until thirst is allayed; then the patient is encouraged to drink freely of plain or carbonated waters for diuretic purposes.

Twenty-four hours after operation we begin to consider the important subject of nutrition. If the stomach is retentive we begin feeding with milk and lime water, equal parts, in amounts of 10 to 15 c.c. every two or three hours. The effect is carefully observed, and if relished by the patient with no signs of nausea or vomiting the amount is gradually increased. Some patients have a great dislike for milk and in some cases it is actually found to be injurious. In such cases we resort to albumin water, beef juice, peptone solutions, or buttermilk, which latter is often very palatable and refreshing. Even if patients relish milk it is well to vary the diet occasionally by giving them one of the above named preparations. In gall-bladder cases the stomach must be carefully watched as regards the tolerance of food, and frequently a case proves a law unto itself. Nutrition must not be forced in the beginning, but a desire for food should be created by skilful attention to quality, temperature, seasoning, and serving. In the first 24 hours of feeding the nourishment given amounts to about 150 c.c. For the next 24 hours we continue the same liquids, only increasing the amount to about 250 or 300 c.c.

If the stomach is retentive we next allow a good chicken broth or beef broth in addition to the milk, so that on the fourth day after operation the patient is taking about 500 c.c. of nourishment. If there are no ill effects, we begin the use of wine whey, wine jelly, or junket, and gradually eggs and gruels are added to the diet. We keep our patients on liquids and soft food until after the removal of the gauze; then we begin on light or carefully selected house diets. In a small percentage of cases patients will require a greater amount of nutrition than has been indicated—in which cases we resort to more frequent intervals, employing, however, the same foods with the addition of alcohol in the form of champagne, brandy, or whiskey. If the stomach is not retentive and vomiting arises as a complication, we stop all food by the mouth instantly, and if the patient is in need of nutrition we resort to rectal feeding. In rectal nutrition the amount should not exceed 150 c.c. The nutritious enemas employed are peptonized milk, peptone solution, and eggs, in such proportions as we deem proper; or an enema that has proved very satisfactory (in that there is better absorption with better tolerance) consisting of 100 c.c. of saline solution with 50 c.c. of predigested and concentrated beef. If necessary some whiskey

or brandy may be added. Such enemas are given at intervals of three to four hours, and continued until the patient is surely able to take some nourishment by the mouth.

In the post-operative management of gall-bladder cases the bowels demand careful attention. In from six to twelve hours after operation we expect a patient to be passing flatus freely, and in this we are rarely disappointed. As a mild peristaltic stimulant we employ suppositories of asafetida 0.3 gram (5 grains) every three hours until there is a bowel movement. In some cases these suppositories sometimes nauseate patients and their use is at once discontinued.

We occasionally meet with cases in which there is very active peristalsis and borborygmus, but owing to a spasmodic condition of the sphincter ani the flatus is not expelled. In such cases the passing of a rectal tube or the inserting of the nozzle of a syringe into the rectum, and allowing it to remain for an hour at a time, will afford great relief. Again, there are cases in which peristalsis is very sluggish and the resulting distention causes very disagreeable symptoms. In such cases we employ an asafetida enema, or one of 50 grams of alum to a liter of water, and the results are often surprising. When paralysis of the muscular coats of the intestine is quite marked, the use of eserine salicylate 0.002 gram ($\frac{1}{30}$ grain) every three hours hypodermatically, stimulates the unstriated muscular fibers and an active peristalsis is established. This drug, when properly employed, is a most reliable therapeutic agent. To obtain the best results it must be used early, because when the muscular coats of the intestines are completely paralyzed by over-distention it is too much to expect any drug to restore the normal tone.

In conjunction with these means of establishing peristalsis, several small, lightly filled ice bags have frequently proved to be of service. Calomel in divided doses is also of considerable value in stimulating peristalsis and has the additional advantage of acting as a laxative.

On the second day after operation we begin to start the bowels. Usually we prescribe divided doses of calomel 0.01 gram ($\frac{1}{6}$ grain) and sodium bicarbonate 0.06 gram (1 grain) every half hour for ten doses. This is followed by a saline—our preference being a saturated solution of magnesium sulphate, but of course there is no objection to citrate of magnesium, Hunyadi water, or other

salines. The saline is given in 15 to 20 c.c. doses every hour until effective, but if there is no result in about six hours, we begin the use of enemas. First we use a simple soap and water injection, which in most cases is all that is needed. If, however, no result is obtained we frequently employ a purgative enema of magnesium sulphate, turpentine, glycerin, and water, given in what we term the "see-saw" method. The enema is given with the foot of the bed raised, and when about to be expelled the head of the bed is raised. This method will prove effective in the majority of cases. Even by the use of such an enema the bowel movement may not be satisfactory, in which case we are in the habit of prescribing castor oil in some palatable form. This old-fashioned remedy has proved very effective in gall-bladder cases, and we have had some very happy results from its use. After the bowels have been opened we desire a daily movement, and to this end, if necessary, we employ such agents as salines or some of the mild laxative pills, always, however, keeping in mind an occasional evacuation by means of castor oil.

We have before called attention to the disposition of the drainage tube. A strict record is kept of the amount of bile drained daily, with its character, and this record is compared from time to time. Sometimes the drainage from the tube suddenly ceases. On examination we may find the tube kinked beneath the dressings or perhaps it may be clogged with inspissated bile or mucus. If such be the case we wash out the tube with warm saline solution, boracic acid solution, or distilled water by means of a syringe. Very little force is used and this is all that is needed to restore the patency of the tube. Besides the tube we have to deal with gauze tampons. When a gall-bladder wound is dressed at the time of operation we employ a layer of gauze wet with 1 to 6000 bichlorid solution, and this is placed directly over the wound and gauze drain. If there is good drainage from the gauze tampons, of course, this first dressing becomes saturated with blood and perhaps bile, but it is this very dressing that should not be disturbed in jaundiced cases in from ten to twelve days. The reason for this is that in gall-bladder cases complicated with jaundice there is a tendency to hemorrhage, and if this first layer of gauze dressing is disturbed very troublesome bleeding may occur from the granulating wound. The dressings above the gauze in contact with the wound may be changed whenever

necessary, and this is always done wherever the dressings are saturated because the odor of decomposing blood and bile is very foul and obnoxious to the patient. Besides the changing of superficial dressings, the wound is not disturbed for ten to fourteen days.

We usually make our first examination on the tenth day, when we note whether the gauze tampons are loose and soft and if the catgut used in retaining the drainage tube appears to be absorbed. If we find things as stated we remove the tube and then proceed to soften the gauze with copious flushings, at a low pressure, of warm saline or boracic acid solution, or plain sterile water. The tampons are thoroughly saturated and then teased one by one until all are removed. Should the tube offer resistance on traction when the gauze is removed it is not disturbed, for perchance the bile may not as yet be perfectly normal in character and the continuation of the tubal drainage for a few days longer will then be of decided advantage. If we find the gauze adhering firmly we do not use hydrogen peroxid, but redress the wound and wait for several days longer because we are not desirous of breaking up adhesions haphazard and run the risk of a peritonitis. Time, patience, and common sense are the factors necessary in the management of gauze tampons.

After the removal of the tube and tampons the wound is lightly packed with iodoform gauze, plain or antiseptic gauze, and this continued until the wound is healed. The dressings take place every other day, or just as often as is required, and are done under antiseptic precautions. In our wound we of course have to deal with a biliary fistula, but this requires no special attention other than is paid to the wound as a whole. The wound is usually healed in from three to six weeks and the biliary fistula closed in from two weeks to six months. The sutures are removed at the time of the first dressing. If the wound heals nicely we allow our patients to sit up in bed on the sixteenth or eighteenth day and a few days later we permit them to use an invalid's chair. Gradually they are allowed their freedom about the rooms or wards, all depending, of course, upon the strength of the patient. In some instances, especially in elderly subjects, it is advisable to get the patient out of bed before the usual time and this is done without any hesitancy, the abdomen, of course, being well bandaged. When the wound is nicely granulating superficially, and if an existing biliary fistula is not of too much annoyance, the patient is discharged—usually in four weeks' time.

SPECIAL CONSIDERATIONS.—*Peritonitis.*—We have not had the misfortune to encounter post-operative peritonitis following gall-bladder operations, even in the suppurative and gangrenous varieties. Our treatment of such a condition would be according to the principles upon which we treat all cases of post-operative peritonitis.

Vomiting.—Vomiting is a very common occurrence after operations upon the gall-bladder and may be looked for in from four hours to three days after recovery from ether. The vomited material varies in color from bile-stained watery fluid to thick, dark grumous matter. Often the vomit is of an exceedingly offensive odor. With a stomach full of such material there is but one remedy and that is the stomach tube. Even when only nausea exists the use of the tube may show the gastric contents to consist of very dark bile and in surprisingly large amounts. The use of stomach sedatives in such conditions is worse than useless, besides being irrational. In using the tube the stomach is washed with liters of very warm water, to which is frequently added sodium bicarbonate, the washing being continued until the water returns clear. At this time we usually introduce a saturated solution of Glauber's salt 60 c.c. (2 ounces) and whiskey 30 c.c. (1 ounce) to aid in correcting any reversed peristalsis, besides effecting a thorough evacuation of the bowels. The influence of gastric lavage in itself serves to set up a peristaltic movement, and this, with the evacuation of foul material from the stomach, is productive of such astonishing results to the patient that if it is necessary again to use the tube, it is welcomed and all the disagreeable features forgotten, because of the great relief afforded. It is often noted that the use of the tube acts better than any nervous sedative, as patients frequently fall into a sound refreshing sleep. We have never had any untoward symptoms, such as collapse or syncope, and we have used this treatment in so many cases with such happy results that our confidence in the stomach tube is well-nigh unlimited.

Hemorrhage.—In cases without jaundice or in those only slightly icteroid we have never encountered any hemorrhage. Even in cases deeply jaundiced demanding operation a preliminary course of calcium chlorid has often done away with this alarming condition. However, hemorrhage will occur in some cases and it proves a most difficult matter to control. As a precaution we have before mentioned the point of not disturbing the primary dressings in

contact with the wound, no matter how saturated they may be. If, however, the oozing and bleeding continue to saturate the superficial dressings without any signs of coagulation, the hemorrhage certainly demands attention. We usually begin the administration of 4 grams (1 dram) of calcium chlorid in starch water by the bowel every six hours, in all cases showing any tendency to excessive oozing. In some cases this will suffice, but in others it does not seem to have the least effect. In such cases we have tried saturating the gauze tampons with a 1 to 5000 adrenalin chlorid solution and also by extra packing with gauze saturated with the same agent. In a few cases we have been successful, but again in others the blood still continued to ooze into the wound. We were able to control one case of hemorrhage with a strong Monsel's solution. Opium has also been given in certain cases, but it has not proved to be of material value. In desperate cases one is tempted to use every known styptic, but even if successful the associated cholangitis and cholemia are usually so grave as to lead to death.

Pain.—The pain following operations varies greatly and depends to a certain extent upon the nature of the case. It is rare, however, that the pain is of such severity as to demand special attention. All patients have pain, but it is a pain that can be borne for the most part and does not call for opiates. A kind, intelligent nurse is a greater power for good than any derivative of opium. We have often noted that in cases complaining of severe pain gastric disturbances are associated and our stomach tube will then afford great relief. Of course, we meet a limited number of cases in which the pain is of such a character as to demand a sedative and then we may order a hypodermic of morphin in doses of 0.002 to 0.005 gram ($1/30$ to $1/12$ grain), if all else fails. Such a small dose does little harm and it serves to take away the keen edge of the pain without narcotizing the patient. Some convalescent patients complain of sharp pain in the region of the operation, especially after the gall-bladder has been anchored to the abdominal wall, but also after cholecystectomy.

These pains, of course, are due to adhesions and are a source of annoyance to the patient, although they are not to be compared with the agonies previous to operation. They may last from one to six months and even much longer, but as a rule they subside in the course of time because the adhesions will stretch or be absorbed.

To facilitate the stretching and absorbing attention to daily and active evacuations of the bowels is necessary and, in addition, abdominal massage has often proved of great service. Some patients, however, will never improve and operative interference may be necessary for relief.

Fistulæ.—Biliary fistulæ are in a number of cases a great source of annoyance. Some fistulæ are closed by the time the patient is convalescing in the hospital, while others exist a year or more before closure. Some may never close, but in such cases there is usually some obstruction and their treatment is operative. In treating a biliary fistula we should not be meddlesome and over-zealous, and continued probing and picking with forceps is uncalled for. Simple light packing with occasional application of nitrate of silver is all that is necessary. Nature will close the fistula in most cases and she must not be interfered with. In speaking of biliary fistulæ we might mention the occurrence of fecal fistula. In cases of extensive adhesions in which the serous surfaces cannot be satisfactorily repaired the presence of the gauze tampons may cause ulceration in the intestine. In a recent case we had a small fecal fistula from the hepatic flexure of the colon, but solid diet and cleanliness closed the opening in a few days.

Jaundice.—Cases with jaundice as a rule clear up very rapidly after operation. However, in a few cases even when the bile is draining freely it has been noted that at times the icterus suddenly becomes more marked and indeed in cases without jaundice a slight yellow tinge in the sclera may be observed. This is probably due to some catarrhal condition. These cases always clear up under the use of cholagogue cathartics and the administration of sodium salicylate in 0.5 gram (7.5 grain) doses three times a day. There are rare cases complicated with severe jaundice in which, notwithstanding the establishing of good drainage, the jaundice increases and the patients rapidly become cholemic. On examining a section of a liver taken from such a case a high grade of cholangitis was observed. The operation *per se* is the remedy for cholangitis, but if this progresses notwithstanding operation, the prognosis, of course, is very grave and treatment is of practically little use. Theoretically, cholagogues are indicated, but we have found them to be of little value. Intravenous transfusion of normal saline solution has given the best temporary results.

Treatment

THE TREATMENT OF PNEUMONIA

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I THINK it may be truly said that there are few diseases the treatment of which has been so completely revolutionized during the last fifty years or thereby as pneumonia. Even later than the early years of the period referred to the chief remedies in common use—and they were often very vigorously employed—were blood-letting, tartar emetic, and, less universally perhaps, calomel and opium. Hot poultices or fomentations were the favorite external applications over the affected side.

The first named of all these was certainly the most interesting and picturesque element in the treatment of the disease; and it opens one's eyes to the possibility of the preservation of life under adverse circumstances to read, as related by Sir William Gairdner,¹ what enormous blood-lettings were practised by the physicians of the older school in Edinburgh and elsewhere, not long before the middle of last century.

The following is a brief summary (for purposes of comparison) of the teaching of the most able physicians of the sixth decade of the last century with regard to the elements of treatment above mentioned:

Blood-letting.—This is a remedy of great power in some cases—as in the very early stages of the acute inflammation, (1) when in unimpaired constitutions; (2) when the disease is attended by inflammatory fever or symptoms threatening life not accompanied by

¹ The Physician as Naturalist, pages 105-108, Glasgow, 1889.

exhaustion, and developed with great rapidity. These must be combined before we bleed, as a general rule; but when they are all combined, we may bleed confidently and freely. The best result is attained when the bleeding is done during the first 24 hours or so of the attack. What happens immediately is relief of the symptoms. An aggravation of the symptoms may come on in some hours, and the patient may have to be bled again; but generally the disease is permanently alleviated and its duration shortened.

Tartar Emetic.—The usefulness of tartar emetic is proved in the same way as blood-letting. It should be given early and largely. It has a wider range of utility than blood-letting; and we are not always debarred from its use when the patient is debilitated, although it must be given in such cases with greater caution. It should be begun with reference to the acuteness of the attack, a liberal dose being a grain every hour or every two hours. Vomiting once or twice after the early doses will do no harm—indeed will rather do good; but if the patient keeps on vomiting or is purged, the dose ought to be diminished; also if he breaks into cold sweat, or if he feels generally uncomfortable and prostrated, we may then diminish the dose by half. This is to be continued till the turn of the disease has been reached, and then all remedial treatment may be stopped (unless the disease recurs) and the patient merely be encouraged to take nourishment.

The side should be poulticed liberally, or hot fomentations may be used: blistering had better be avoided. In some cases opium may be employed as a palliative, but the routine use of opium with calomel is not to be recommended. Some mild cough mixture may be given, and alcoholic stimulants (which are not opposed to the use of tartar emetic) are required when the vital powers seem to be failing.

The older physicians clung very tenaciously to the antiphlogistic idea in the treatment of acute diseases, and in none more, perhaps, than in pneumonia. But now the theory underlying the employment of so-called antiphlogistic measures is quite forgotten, or only regarded “as part of the historic lumber of a remote past;” and even blood-letting, which in rare cases of pneumonia (as also of some other diseases) may be a power for good, is now hardly ever practised. The swing of the pendulum has perhaps carried us rather too far in that particular.

So far as drugs are concerned, I have seen only a very few cases of pneumonia treated in the old-fashioned manner. The place of active treatment has gradually been taken by what may be called the expectant method. And this is based upon the fact that nothing will *cure* the disease, that it is spontaneously curable in most cases, and that the aim of the physician must be to act the part of a skilful pilot until the crisis of the attack is reached.

I think it is now almost universally recognized that the key of the position lies in the capability of the heart to carry on its work in its handicapped conditions; and in this connection the evil effects of high temperature, and that which causes it, upon the heart muscle must not be forgotten. At the same time it must be admitted that cases not infrequently prove fatal in which there has been no very high temperature.

The main indication, therefore, should be met by adopting a method of treatment which, whether it be stimulating or tonic, is *not* depressing; and to this end ammonia and ether, quinin and strychnin seem to me to be most useful so far as drugs are concerned.

Even in the face of a high degree of temperature, antipyretic drugs are worse than useless on account of their depressing action on the heart (which is just the thing we wish to avoid); and we have a much better means of checking or reducing what we may consider a dangerously high degree of pyrexia in the application of cold to the surface, either by the ice-bag, the cold wet pack, or, in extreme cases, the cold bath.

I am not in favor of the use of digitalis, as it seems to me to be often responsible for the nausea which prevents the patient from taking food, or even for actual vomiting, and therefore it acts as a depressant. I am bound to admit, however, that its use is very popular. I have seen very few cases of acute pneumonia in consultation in which it was not being given, and I have always advised its discontinuance on account of the view above expressed. The attention of those whose opinion and practice differ may be directed to the results of an experimental inquiry carried out by Sir T. Lauder Brunton and Professor Cash, of Aberdeen University, on the "Alterations in the Action of Digitalis produced by Febrile Temperature."¹ The conclusion arrived at in this inquiry is to the

¹ The Practitioner, vol. xxxiii, p. 272.

effect that a high temperature lessens the inhibitory power of the vagus center in the medulla to such an extent that digitalis, which acts on this center, loses its power, to a great extent, to restrain the action of the heart and slow the pulse, as it would at the normal temperature, and that at a very high temperature it might have no such effect at all. These observers add: "It is therefore evident that digitalis and its congeners, if they are given at all when the temperature is high, should be given with great care, for otherwise the medical man may be induced, by the apparent inaction of the remedy, to push its administration too far during the fever, with the consequence of producing too great depression of the pulse during defervescence." I think it is much the safest course not to give such drugs at all.

For the distressing stitch-like pain accompanying pneumonia which is of course pleuritic, I have never seen anything act so effectively as the application of two or three leeches, and these may be followed by either hot or cold applications, according to circumstances. Opium is to be avoided; and I cannot remember ever to have prescribed its use since I have had to treat cases of pneumonia on my own account. I have been always shy of using it in almost all affections of the lungs (hemoptysis, however, being a notable exception); and as regards pneumonia, I am glad to find myself in accord with Sir William Gairdner, who writes as follows:¹ "In regard to one of these remedies, I shall put in a final word of caution founded upon experience, because I have observed that men of the highest rank, and to whom my feelings are those of the greatest respect, have written upon the subject, as I should say, incautiously. Opium is in my view a very dangerous remedy in pneumonia, and specially dangerous even in the most moderate doses about the period when the crisis may be expected. The danger consists in the very marked tendency this drug has to cause increased cyanosis and collapse, probably from its paralyzing action upon the respiratory center."

But I believe very strongly in the benefit, in many cases, of the hydrotherapeutic method of treatment, especially when a considerable degree of pyrexia, say 103° F. or over, is associated with

¹ The Practitioner for January, 1900.

delirium; and I may mention a case occurring to me a few years ago which illustrates this point.

It was that of a carter, aged 28 years, addicted to the abuse of alcohol, who was admitted to the hospital under my care, having been seized four days previously with cough, pain in the right side of the chest, and vomiting. He looked older than his stated age, had flushed cheeks, a restless expression, and was delirious. His respirations were quick and shallow and his expectoration blood-stained. When I first saw him his temperature was 101.2° F.; pulse, 120; respiration, 44. He had all the usual physical signs of pneumonia of the right lower lobe. Next day it was noted that he had slept none, and that he had been delirious and noisy. At 8 P.M. of the day after admission his temperature was found to be 104.2° F.; respiration, 58, and pulse, 140. He was almost unrestrainable; and when I reached the hospital on a special summons at 9 P.M., I found that it had been thought necessary to apply the restraining sheet. There being no suitable bath available, I ordered the cold wet pack. He was wrapped in sheets wrung out of iced water, pieces of ice were placed over him, and cold water was poured over the sheets, the water running off the bed (a mackintosh having been placed under him) into a tub placed at its foot. In an hour the respiration rate had sunk from 58 to 42 and the pulse to 92. Temperature unreliable, as it could only be taken in the axilla, but there it was 96.4° F.) Shortly thereafter the pulse was found to be 92, the respiration 36, but some delirium was still present. At 6 o'clock next morning the temperature was 101.6° F., at 10 A.M. it was 99.6° F., at 4 P.M. it was 102.8° F., the delirium having begun to abate. From this point the temperature steadily fell, being 101.2° F. at 10 P.M., and at 11 he fell asleep. Next morning it was noted that he had slept well and was quite sensible, temperature, 98.8° F.; pulse, 112; respiration, 40. Physical signs over the right lower lobe were much as before, with the exception that there were abundant *redux* crepitations audible. He was quite convalescent in about ten days, and was discharged after the lapse of about ten days more.

This patient on discharge from the hospital returned to his old habits, notwithstanding ample warning, like the proverbial "sow that was washed to her wallowing in the mire," with the result that he was attacked again, about a couple of months later, by pneumonia of the other base. His attack seemed on all fours with the former

one; his temperature rose to 104° F., was not checked by cold applications, and he rapidly sank and died.

Now, of course, no one can say that the difference in treatment was the cause of the different result, but the facts supply food for reflection.

Another patient with a temperature of 105° F., whom I treated with the cold bath,¹ although not delirious, suggested to me the usefulness of that method of treatment in face of a high degree of fever even without delirium. The patient was an errand-boy, aged 17 years, who came under treatment on July 22, and had been at work up to the previous evening. At 6 A.M. of the day of admission he was seized with a "catching" pain in the left side of the chest, followed by a severe rigor. He was a delicate looking lad with sallow complexion, and complained of headache as well as of pain on deep inspiration. His temperature was 101° F.; pulse, 102, full and bounding, and respiration, 28. The tongue was slightly coated but moist; the skin hot and pungent; the thorax well formed; resonance over the chest, and the breath sounds and heart's sounds also normal. At 8 P.M. the temperature was found to be 105° F., and he was put into a bath at a temperature of 80° F. for ten minutes. An hour later the temperature was 103.4° F., but at 10 P.M. it had risen to 104° F., and at 11 it was again 105° F. The bath (at 75° F.) was again employed for ten minutes, and in half an hour his temperature was found to have fallen to 103° F. Next morning (July 23) impaired resonance was detected over an area about the size of the palm of the hand about the middle of the left back, together with tubular breathing, bronchophony, and fine crepitations. He had also commenced to expectorate faintly rusty sputum, and his temperature about midday reached 105.2° F., at which he had a third bath, followed by the application of an iced-water coil to the left chest; and for internal medication a mixture containing ether and ammonium carbonate, with a small allowance of brandy. The bath reduced his temperature by 3° , but by 6 P.M. it had advanced to 104.4° F., falling three hours later to 102.2° F. The pain was then much relieved; but his cheeks were still flushed, and his tongue dry and brownish. On July 25 the urine showed a trace of albumin; in the evening the temperature was 98.6° F.,

¹ Reported in the British Medical Journal for January 14, 1882.

and at midnight, 97.2° F. Next morning (26th) it was 99° F.; pulse, 88; respiration, 24. No moist sounds were audible over the affected area, the breath sounds were tubular but feeble; there was less dulness on percussion, and no pain. The following day's note showed that the pneumonic patch had all but cleared, and the sputum was mucopurulent. Convalescence was completely established a few days later, and the patient was in due time sent to a convalescent home.

Although in this case there were at first none of the more definite signs of pneumonia present, there could be no doubt as to the pyrexia, and the desirability (in my judgment) of reducing it; hence the bath. The pyrexia lasted exactly three and a half days, calculated from the rigor; and while defervescence sometimes occurs (perhaps especially in young subjects) as early as this in cases otherwise treated, or not treated at all, the point in this case is sufficiently noteworthy to raise the question whether it might not have been due in some measure to the use of the cold bath. In any case, looking to the enormous benefit obtained from the bath in the hyperpyrexia of acute rheumatism and enteric fever, it seems fair to expect a similar result in the high temperature of some cases of pneumonia.

As regards the ice-bag, it has been claimed that it checks the inflammatory process in the lung. It may be so; but I have never been able to satisfy myself that it acts in any other way than as a local refrigerator, the local effect passing necessarily into one of general reduction of pyrexia. Even acting in this way, it may often be very useful.

I have had no experience in the use of hypodermic saline injections, and I am not, on various grounds, much attracted to try them; but the method has been well reported of from the Johns Hopkins Hospital, which is a point in its favor.

Theoretically, the inhalation of oxygen ought to do good. I have, however, never seen any permanent benefit resulting from its use. Possibly the reason for this may lie in the fact that one only thinks of it in the very worst cases and as a last resort.

As a remedy for sleeplessness, cold or tepid sponging is the safest; but in the event of that failing, chloralamid may be thought of; although it should be remembered that the less drugging we have recourse to the better.

Nothing special needs to be said about dieting. As to general management, capable nursing is of great importance. The patient should lie on a hair mattress, at the side of the bed most convenient for the physical examination of the affected side, and with a light covering of blankets while pyrexia lasts. He should have as few people about him as possible, should not be encouraged to talk, and should not have his sleep disturbed for the administration of food or medicines.

The chief points of the foregoing may be summarized in the following propositions:

1. No routine drug treatment is of any practical value.
2. Antipyretic drugs and all depressing lines of treatment are especially to be avoided.
3. The same may be said of nauseating drugs, such as tartar emetic, and even digitalis, which is indirectly depressing, because it induces impairment of appetite and nausea (if not actual vomiting), and so interferes with nutrition, which again tends to cause heart failure.
4. A supporting and, in the widest sense, stimulating line of treatment will be found to give the best results.
5. For relief of the pleuritic pain, nothing is so good as leeching.
6. In the presence of high temperature, refrigeration to the surface by the ice-bag locally or by cold water generally is desirable—the latter especially, and applied assiduously, if delirium be a complication.
7. In the case of vigorous subjects when cyanosis is present, and there is obvious engorgement of the right heart, general blood-letting may with advantage be practised.
8. Alcohol should not be prescribed in a routine way. When it is clearly required by a consideration of the pulse, temperature, and tongue, it is invaluable, and it should be given (as regards quantity) in proportion to the age and other conditions of the patient calling for its employment.

Finally, as to the results of different methods of treatment, we have all need to bear in mind what is so well expressed by Professor Osler. Under the head of *Special Treatment*¹ he says,

¹ The Principles and Practice of Medicine, fourth edition, p. 134.

“Certain measures are believed to have an influence in arresting, controlling, or cutting short the disease. It is very difficult for the practitioner to arrive at satisfactory conclusions on this question in a disease so singularly variable in its course. How natural, when on the third or fourth day the crisis occurs and convalescence sets in, to attribute the happy result to the effect of some special medication! How easy to forget that the same unexpected early recoveries occur under other conditions!”

THE MEDICAL TREATMENT OF GASTRIC CANCER

A CLINICAL LECTURE

BY ALBERT ROBIN, M.D.

Physician to the Paris Hospitals

GENTLEMEN: The subject of this lecture may appear to you to be strange when we consider that gastric cancer is an incurable lesion; but I wish to-day to point out how you ought to and can improve the situation of these unhappy patients. One of the facts that made the greatest impression on me in the beginning of my medical studies was the lamentable way these patients were abandoned. I noticed the greatest physicians, such as Béhier, manifest a sort of powerless indifference toward them; milk diet was prescribed, injections of morphin were given when the suffering became intolerable, and perchlorid of iron was administered for hematemesis. That was all!

This was not sufficient, and in the presence of the physicians' apathy the surgeons have taken up the treatment of cancer, both curative and palliative, so that at the present time three-quarters of the cancer patients that enter the hospital undergo one or other of the following operations: pylorotomy and gastrectomy, on the one hand, and gastro-enterostomy on the other. It therefore seems to me that it is well to protest against this situation and to warn you against such an excessive tendency. This is why I wish to speak to you to-day about the medical treatment of cancer. Later on we shall see in what conditions and under what restrictions surgical intervention can be resorted to.

The treatment of gastric cancer has two aims: (1) to lessen the patients' suffering, and (2) to feed them and prolong their lives as much as possible. Let us now see how this can be accomplished.

You must keep before these patients' eyes a hope of recovery, and, as a general rule, treat them without preconceived opinion, in the same way that you would treat patients suffering from curable complaints that you might take for cancer. You should therefore follow out a collective treatment, which in many cases,

even when there does not appear to be the shadow of a doubt, will enable you to effect the most astonishing improvement. I observed a few years ago a typical instance of this sort. The patient was a man with the classical symptoms of gastric epithelioma: black vomiting, tumor, loss of flesh, cachexia, etc. Guided by the rule that I have just mentioned, I made no final diagnosis, but put into effect the collective treatment of the patient's condition, and two months later he left us entirely cured! It was therefore a false cancer, and I have no doubt that a mere milk diet would have given a very bad result in this instance. The medical treatment of gastric cancer is therefore more complicated than you may think, as I shall now proceed to show you.

In the first place, there is no use in counting on any of the specific treatments, in which some physicians have believed. Thus, about thirty years ago Cabazès brought forward the use of white condurango as a specific for cancer, and Trives reported that this remedy had given 4 recoveries out of 51 cases in his hands. These results are not certain, but, nevertheless, condurango is a useful remedy as a stimulant to the appetite and digestive functions. It can be given either as a decoction, extract, or tincture. The decoction is prepared as follows: Add 15 grams of condurango bark to 250 c.c. of boiling water; concentrate to 150 c.c., filter, and add 1 c.c. of pure hydrochloric acid. This preparation can be given in doses of from three to four tablespoonfuls a day, before meals. The extract is given in doses of 10, 15, to 50 centigrams (1.5 to 8 grains), and the tincture in doses of 10, 20, to 50 drops (0.6 to 3 c.c.) per diem. The second drug that has been held in high favor since the paper published on the subject by Brissaud in 1893 is chlorate of sodium. For some time previously chlorate of potassium had been used in epithelioma of the tongue and skin. Brissaud did not choose chlorate of potassium, because this substance is a poison for the blood, transforming oxyhemoglobin into methemoglobin, and because large doses must be used. In his paper he mentions five patients who had taken from 8 to 16 grams (2 to 4 drams) of chlorate of sodium a day; under the influence of this treatment the patients were relieved, the cachexia disappeared, in one case even the tumor was dissipated in six weeks, while the melena and hematemesis ceased.

It was therefore claimed that chlorate of sodium had a specific

action on gastric epithelioma. However, my own experience, as well as that of several other writers, has been that this substance acts as a tonic, and merely increases the patients' strength, stimulates their appetite, and facilitates their digestion. In any case, although chlorate of sodium is not a specific, it is a useful remedy that deserves to be retained as a means of favoring intestinal digestion, with which these patients are able, up to a certain point, to replace their defective gastric digestion. It is well to add that chlorate of sodium is never to be used when there is even a slight trace of albuminuria.

A number of other substances have been advanced as specific remedies for cancer, but I can only mention the principal ones:

Bichromate of potassium was advised by Vulpian, but it is inferior to condurango and chlorate of sodium; it may bring on gastric irritation and make the patients' condition worse. Therefore do not use it.

Tincture of *thuja occidentalis*, which was celebrated in its day, was advanced as a specific remedy in doses of four drops per meal, increasing one drop a day up to a hundred drops. Under the influence of this drug the patients increase in weight, but it acts simply as a tonic, from which point of view only it deserves to be remembered and applied to the relief of cancerous patients.

The extract of *chelidonium majus* was recommended by Gressensko to cure cancer in general, either in local applications to external cancers, such as that of the breast, for instance, or for internal use against the cancerous diathesis. I have never obtained any good result from its use, and I do not advise you to try it.

Another plant of the same family as the condurango, calago, which is used by the Paraguay physicians, has been brought forward of late years. It is a bitter tonic that is useful in increasing appetite, and it enables you to vary your remedies for that purpose. This is a point not to be despised in the treatment of cancerous patients, with whom the efficacy of drugs is quickly exhausted.

I must now merely mention some other substances, such as sulphate of anilin, 5 to 10 centigrams (0.8 to 1.5 grains) a day, which should not be used, as it lessens appetite; pyoktanin, whose action is about the same; chlorid of gold and sodium, bromid of gold combined with arsenate of sodium and with alkalis. These substances all unfavorably affect the gastric mucous membrane.

There still remains the important question of the serums, of which we now have two kinds: those of Wichet and Théricourt, and of Baylac, to which must be added de Backer's yeasts.

Wichet and Théricourt's serum was tried in our wards on a patient suffering from gastric hyperesthesia with pyloric stenosis and hyperchlorhydria. This was a remarkable case, as analysis showed 3.5 grams of hydrochloric acid. I do not know of any case to compare with this, except one observed at the Pitié Hospital, where there were 1.5 grams of hydrochloric acid. Out of the 15 or 20 cases of gastric cancer accompanied by hyperchlorhydria that have been published, the hydrochloric acid never rose above 1.75 grams and was often as low as 0.75 gram. The patient left the wards cured, but are we certain that the case was one of cancer? In two other cases the serum gave no results.

As regards the second serum, which was the subject of a paper read by Lucas-Championnière before the Academy of Medicine, it does not seem destined to give any better results than the foregoing one.

Finally, M. de Backer's yeasts have had no positive effect in my hands.

Therefore the serum question has not yet reached any definite point, although it is quite possible that it may do so at some future time. In a word, all the remedies proposed as specifics for cancer are to be regarded as tonics and stimulants. A practical, curative treatment by medical means does not exist, and we shall see, after a while, what we are to think of surgical treatment.

But let us return to the palliative treatment of cancer. The patient must be fed, the leading symptoms must be relieved, and cachexia must be retarded as much as possible; this is all the more important in that we shall presently see that the medical treatment can be very well combined with the surgical treatment, as a preparatory means toward the latter, to increase the patient's power of resistance, and to enable him to withstand an operation without too much risk.

Cancerous patients can be divided into three categories, according to which of the three following diets they are put upon: (1) Absolute milk diet; (2) mixed milk, vegetable, and animal diet; (3) mixed vegetable and animal diet without milk.

Let us see which patients are to be placed in each of these categories.

(1) *Absolute milk diet.* This class includes (a) patients with pyloric stenosis, who are about three in ten cases; (b) those who have just had a hemorrhage; (c) those who have hemorrhages that do not yield to the usual treatment, which I shall point out presently, and (d) absolute milk diet is indicated, but as a temporary means only, in every case when there is vomiting.

(2) *The mixed milk, vegetable, and animal diet.* When the gastric contents of a cancerous patient are examined, the most striking feature is the almost total disappearance of hydrochloric acid, and the non-digestion of albuminoid food; all that you find is a little syntonin, or propeptone, and a few infinitesimal traces of peptones, the greater part being pure albumin, which can be coagulated by heat. On the other hand, you find that starchy foods, given in small quantities, are well digested.

At first sight the inference to be drawn from these facts would seem to be that animal food ought to be completely forbidden in these patients. We must not forget, however, that the intestine can take, to a large extent, the place of the gastric function, for into the intestine flow both the pancreatic secretion, which contains three ferments, of which one digests albumin, the second starches, while the third turns fat into an emulsion; the bile, which also turns fat into emulsion, and the intestinal secretions, which contain the inverse ferment that acts on sugar. Consequently, when the intestine is in good condition it is quite capable of taking the place of the stomach. If, however, you are dealing with a patient with a bad intestine, which you can recognize by the existence of gurgling sounds, flatulence, diarrhea, or constipation, if the patient is not comprised in the first class he should be put on the vegetable and milk diet, as the cancerous stomach still digests most of the vegetables. You should prescribe this diet as follows: In the morning, on awakening, a pint of milk taken slowly; at 11 o'clock, a meal in which milk should be taken as drink and at which the patient should eat different vegetables, particularly those that are more nourishing, such as peas, lentils, and beans, together with alimentary pastes, —macaroni, noodles, etc.; at 4 o'clock, milk again, and at 7, a meal similar to that taken at 11. By means of this diet you will succeed in improving your patients' condition and in getting them to put on weight.

I must now say a word about the use of another class of foods

with these patients—those that prevent waste. The best is gelatin, or gelatinous articles, such as meat-jelly, calf's-head, and sheep feet; to some patients you can give young meat, such as pullets, lamb, and veal; do not be afraid to give spices, mustard, pepper, salt, pickles, anything that will excite appetite without bringing on any gastric attack.

All that I have said applies to patients of the second class; these patients, therefore, must take with their milk nitrogenous vegetables and a little meat jelly to prevent waste of the albumin of the body.

The patients of the third class are those who have good intestinal digestion; it is in such cases that the best results can be obtained by suitable diet, it being possible to increase their weight sometimes from 4 to 12 pounds. The *régime* on which I put them is as follows: They should take, on an average, five meals a day. First meal, 8 A.M., 200 c.c. (7 ounces) of milk, with a little tea or coffee, and 30 grams (1 ounce) of toast with butter; second meal, 10 A.M., 100 grams of brains or sweetbread, 2 soft-boiled eggs, 50 grams of toast with butter, and a little ham hash; third meal, noon. 6 oysters when in season, 150 c.c. of milk and rice, a small cup of meat juice, 50 grams of macaroni, bread; fourth meal, 3 P.M., 150 c.c. of tea and milk, and a small cake; fifth meal, 8 P.M., 100 c.c. of cream, 40 grams of hashed ham, half a whiting, toast and butter.

This bill of fare, which, on account of its variety, is generally well accepted by the patients, represents exactly the number of calories necessary for an adult—65 kilos in weight—to keep him in good condition. This diet, with the help of laxative remedies, and of such remedies as may be necessary to treat the leading symptoms, enables us to obtain in 40 per cent. of these cases marked improvement, with increase in weight.

Such is the dietetic treatment of gastric cancer. I now pass to its pharmaceutical treatment, which is designed to relieve the predominating symptoms, or accidents, that may occur in the course of the disease.

The commonest symptom of all, and the one that immediately draws the physician's attention toward the possible existence of cancer, particularly in a man of a certain age who at the same time loses color and flesh, is loss of appetite, soon followed by positive distaste for food. This is a most distressing symptom, but if you

know how to handle the different means we possess you will almost always be able to reawaken with ease a feeling of appetite in these unhappy patients. This question of how to awaken appetite in a patient who will not eat, applicable to all pathologic conditions in which anorexia appears as a predominating symptom, is important, and I shall therefore go into it in some detail.

The means used for stimulating appetite are countless, and differ in their nature and strength; they can be divided into three classes, according to which of the three following indications is to be met: slight loss of appetite, great loss of appetite, or absolute loss of appetite.

In the first case the remedy with which I begin is quassia amara; a few shavings should be put in a large glass of water at night, and the following morning the patient should take one or two Bordeaux-glassfuls of the maceration. Very often this means succeeds.

If in a week's time the appetite has not returned, I resort to the *menyanthes* plant, or water clover, which is usually given in infusion or maceration, but which I prefer to prescribe as a tonic, prepared as follows: put 5 grams of *menyanthes* in a cup, pour in 100 c.c. of boiling wine, and filter in 20 minutes. This preparation, which is extremely active as an appetite stimulant, should be taken in doses of a tablespoonful half an hour before meals. Remedies of this nature are best taken between meals.

If these two remedies do not act, tincture of St. Ignatius' bean, tincture of false angostura, or tincture of *nux vomica*, in doses of 4 to 6 drops, 15 minutes before meals, may be used.

When there is great loss of appetite I give, a quarter of an hour before meals, a wafer containing 25 centigrams (4 grains) of chlorid of ammonium, 10 centigrams (1.5 grains) of Dover's powder, and 25 centigrams of bicarbonate of sodium. The chlorid of ammonium acts as a stimulant, and possibly favors the secretion of hydrochloric acid. Or I prescribe:

R	Sulphate of potassium,		
	Nitrate of potassium,	of each	1 grain
	Powdered ipecac,		$\frac{1}{3}$ grain
	Bicarbonate of sodium,		5 grains
			0 05
			0 02
			0 30

The potassium salts act as osmotic stimulants, the ipecac as a dynamic stimulant, and the bicarbonate of sodium as a physiologic

stimulant. Two or three centigrams of nux vomica powder can be added to this formula.

A third preparation, that is useful in such cases, is the following, which acts both by its bitter taste and by the stimulating properties of the substances it contains:

Condurango bark,		
Menyanthes,		
Theriaca,	of each 10 grams	150 grains
Infuse for two hours in		
Quassia wine,		
Calumba wine (boiling),	of each 125 c.c.	4 ounces

Shake the mixture from time to time while it is infusing, add 40 drops of tincture of nux vomica, and filter. In this way a wine is obtained that keeps very well and has strong appetizing properties; this preparation can be specially kept for cancerous patients.

In more serious forms of anorexia wonderful results can be obtained from two new drops to which I have lately called attention, the persulphate and metavanadate of sodium. The first of these is given in doses of a teaspoonful of the following solution half an hour before meals:

Persulphate of sodium,	2 grams	30 grains
Distilled water,	300 c.c.	10 ounces

Each teaspoonful contains 10 centigrams of the salt, and this dose, given twice a day, should never be exceeded; furthermore, the remedy should be stopped as soon as the appetite reappears. If these two rules are not followed, bad results may be obtained, such as a disagreeable and painful sensation of hunger; when, on the contrary, the persulphate is used in the proper way, as indicated above, it succeeds in about two patients out of three. This remedy had been successfully used in tuberculosis, particularly in Lyons, but it was soon found that it only acted as an appetizer, and that it was by stimulating the digestive function that it improved the consumptive patients' condition.

The metavanadate of sodium is a still more energetic remedy, and should be substituted for the preceding one if no results have been obtained in a week's time. As was the case with the persulphate, it was used in the first place in tuberculosis, but it has ended by being considered a remedy for loss of appetite. It is a dangerous

poison, and must be handled with great care. You should never give more than two milligrams ($\frac{1}{30}$ grain) a day, never continue it for more than eight consecutive days, and, finally, its employment should be discontinued as soon as the effect is produced. I use the following formula:

Metavanadate of sodium,	0.03 gram	$\frac{1}{2}$ grain
Distilled water,	150 c.c.	5 ounces

Each teaspoonful (5 c.c.) corresponds to 1 milligram, and this dose should be given to the patient half an hour before luncheon and dinner.

With the gradually increasing activity of these different preparations you will succeed in awakening the appetite of about half of your cancerous patients; but this is not all, as you must get them to digest what they eat. These patients secrete no more hydrochloric acid and very little pepsin or lab-ferment; they have difficulty even in digesting milk. It is in these cases that excellent results can be obtained from the judicious administration of hydrochloric acid and pepsin.

I use a two per thousand solution of hydrochloric acid, and direct the patient to drink a Bordeaux-glassful in a number of swallows during a meal. Let me call your attention to this detail, because it is important. You must try as closely as possible to place your patient in the conditions of natural digestion; now, in the latter the hydrochloric acid is secreted gradually as the digestion of food proceeds. Consequently your solution should be introduced little by little into the stomach, and not in a single dose at the end of a meal. These remarks apply equally to pepsin, of which I give from 3 to 5 of the following wafers at intervals during the course of the meal:

Pepsin,	0.30 to 0.40	5 to 6 grains
Maltine,	0.10	1.5 grains

As a rule, far too little pepsin is given by physicians. A normal stomach secretes large quantities of it, and we should have to give hundreds of grams if we intended to replace exactly that which could be produced by a healthy organ. Consequently, always give at least several grams of it. You can at the same time prescribe

pancreatin, but in separate and protected pills, that will go through the stomach and be dissolved only in the intestine. You can thus administer two or three pills of 10 centigrams each at the end of the meal.

In this way you may succeed in accomplishing artificial digestion of food; but when the latter is accompanied by abnormal fermentation, causing pain, you must try to prevent the latter.

The treatment varies; you must first try to ascertain to what type the fermentation belongs. When it is lactic, give the fluorid of ammonium, which has no action on soluble ferments. Thus, in the middle of a meal your patient can take a tablespoonful of the following:

Fluorid of ammonium,	4 grains	0.25
Distilled water,	10 ounces	300

When the fermentation is butyric, use erythrol; give in the middle of a meal one of the following wafers:

Erythrol,	$\frac{1}{8}$ to $\frac{1}{3}$ grain	0.01 to 0.02
Calcined magnesia,	$1\frac{1}{2}$ grains	0.10

When neither of these preparations act, try iodized sulphur, which is a very good remedy for flatulence; give 10 centigrams in a wafer at the middle of a meal.

Such is the treatment of anorexia, dyspepsia, and gastric fermentation in cancerous patients.

There is another symptom, much less common with these patients than in gastric ulcer, but still which is present; I refer to pain. One of the best means of quieting it is to apply to the epigastrium a plaster composed of theriaca, extract of belladonna, hemlock, and acetate of ammonium. A second means is to apply to the epigastrium a small blister, and, when the epidermis has been removed, to dress it with 10 centigrams of opium powder. In the third place, try lime water, combined with codein and cocain, as follows:

R Hydrochlorate of cocain,		
Codein,	of each 1 grain	0.06
Lime water,	5 ounces	150 c.c.
Give a dessertspoonful (10 c.c.) when there is pain.		

On the other hand, you must know that in many cases the pain is due to the acids formed by gastric fermentation, and that then

the best treatment is the use of strong saturation powders, such as this:

R	Lactose,	15 grains	1 0
	Calcined magnesia,	23 grains	1 50
	Bismuth subnitrate,		
	Prepared chalk,	of each 10 grains	0 70
	Codein,	$\frac{1}{2}$ to $\frac{1}{8}$ grain	0.005 to 0 01
	Sodium bicarbonate	15 grains	1 0

For one powder (the lactose merely prevents the powders from caking).

The reason why I prefer codein to morphin is that the former has a special sedative influence on the solar plexus, which is, if not the origin, at least the center of the pain in gastric cancer; whereas morphin acts specially on general sensation. The results obtained justify these provisions. These powders should be taken with a little water at the moment when the patients feel the beginning of pain and complain of cramps, pyrosis, etc.

The last accident that I have to speak to you about is hemorrhage. This symptom has not in cancer the same importance as in gastric ulcer, but still it is a drain on the patient, and you must try to prevent and stop it. The vomiting in these cases usually resembles coffee-grounds. To check such a hemorrhage you should use the means indicated to you when I spoke of the symptom hemorrhage in gastric ulcer; but it is not impossible to prevent a hemorrhage, and if when a patient vomits, and in examining the matter you perceive black or bloody shreds, it is probable that a serious hemorrhage is imminent. You should then prescribe:

R	Tannic acid,	4 to 8 grains	0.25 to 0 50
	Opium powder,	$\frac{1}{8}$ grain	0 02
	Calcined magnesia,	1.5 grains	0 10
	For a wafer. One before each meal.		

This remedy, which does not irritate, is well tolerated and succeeds.

In other cases vomiting is a necessary symptom, as it were, and is due to pyloric stenosis; these patients naturally belong to the surgeon. But when the stomach is not distended, and vomiting occurs, you should treat it by means of the plaster I mentioned above, by cocain and codein combined with lime water, and by powdered opium applied to a blister. All these means, used for pain,

are also excellent in vomiting. You can also use the following preparation:

R	Picrotoxin,		
	Hydrochlorate of morphin,	of each $\frac{3}{4}$ grain,	0.05
	Sulphate of atropin,	$\frac{1}{6}$ grain,	0.01
	Ergotin,	15 grains,	1
	Cherry-laurel water,	3 drams,	12
	Dose, 5 to 6 drops ten minutes before eating.		

Finally, if none of these remedies stops the vomiting, you will have to give up solid food and put the patient on a milk diet.

Such are the indications and the rules for the medical treatment of gastric cancer which has given me the following results: Out of 25 patients, 10 increased in weight and benefited both as regards prolongation of life and the symptoms that occurred. The increase of weight varied from $3\frac{1}{2}$ to 12 pounds; the minimum was 1 pound. The average length of time during which they survived was 422 days.

Let me now say a few words concerning the three surgical operations performed in this disorder, and which must be considered from the point of view of the operative risk, improvement in symptoms, and length of time the patient survives.

Taking, first, pylorectomy and gastrectomy, and considering only the statistics of the last few years, we find that the percentage of deaths, which was originally 60 per cent., has been reduced to from 30 to 35 per cent. As regards their results, we find that the surgeons obtain great amelioration and an increase in weight that exceeds that obtained by medical treatment. Several patients gained 22 pounds, and their digestion was much improved. One patient could assimilate 125 grams (4 ounces) of meat a day four months after the operation, and his assimilation of fatty substances was normal; another patient still had distaste for meat and sugar, but ate starches and fatty substances with pleasure. Finally, survival is longer after an operation than after medical treatment, but I only refer to pylorectomy, as the cases of gastrectomy are, so far, too few in number. The average survival was 507 days. Some statistics give results that are almost incredible; thus, Hofmeyer says that 24 patients survived from two to eight years, and in quite recent statistics there are mentioned one survival of ten years, one of eight, one of seven, and three of four years.

This treatment is, therefore, better than the medical treatment; consequently, whenever a diagnosis can be made early enough, advise pylorotomy. It is a curious fact that this conclusion would not to-day be approved by the majority of surgeons, as there now seems to be a current of opinion in favor of gastro-enterostomy. The death-rate from this operation was about 60 per cent. ten years ago, but has now been reduced to about 35 per cent.; on the other hand, the improvement effected by it is only temporary. The patients' color remains cachectic, as opposed to what happens in pylorotomy, and the average survival is only 209 days, consequently only half of what we get with the medical treatment. In a word, this operation, in which the danger is slightly greater than in pylorotomy, only gives temporary relief for the pain, which can be quieted otherwise, and the patients only survive half the time they do when treated medically.

Consequently the question is settled: When a radical cure like pylorotomy is impossible, I think you had better not operate, and that you should only have recourse to gastro-enterostomy in exceptional cases, to quiet severe pain that resists other means. Such are the conclusions to which I have been led both by my personal experience and by the study of the principal statistics that have been published in the last ten years.

CARBONIC ACID TREATMENT IN RECTAL DISEASES

A PAPER READ BEFORE THE AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION IN
WASHINGTON, D. C., MAY, 1903

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THE application of carbonic acid gas externally was very popular among the English and the French physicians of the eighteenth century. They praised the effect on ulcers, especially scorbutic, cancerous, and phagedenic ulcers, and described its hyperemic effect on mucous membranes. During the middle of the nineteenth century, Verneuil, Broca, and Demarquay, in France, and Simpson, in Scotland, made extensive use of it in gynecologic and surgical practice.

For some time the gas was discredited in consequence of an error by Scanzoni. He was under the impression that the entrance of carbonic acid gas into the uterine cavity had caused death in a certain case. The experiments of Claude Bernard and other French investigators brought conclusive evidence that Scanzoni was in error; notwithstanding, the error is alive yet, and for this reason I may be permitted to quote from a former publication of mine, to prove the truth about the harmlessness of the gas. This quotation may appear the more excusable when we read, for instance, in the latest edition of Eulenburg's "Realencyclopædie": "When carbonic acid has been introduced in large quantities into the cavities of the body, as for instance the uterus, the intoxication produced thereby may become fatal by asphyxiation."

Röhrig's experiments on rabbits have shown that considerable masses of carbonic acid gas may be introduced in the veins without producing symptoms of intoxication. Demarquay injected within 40 minutes one liter of the gas into the crural vein of a dog without causing any change in the well-being of the animal. Breslau and Vogel inflated the vagina of pregnant rabbits with carbonic acid gas without harm to the life of either rabbit or fetus. My own experience furnishes additional evidence.

The processes of double gas exchanges, of oxygen and carbonic acid, in our system are not yet sufficiently explained. The question which is yet to be solved is, Does the exchange of these gases take place in consequence of the difference between their tensions in the blood and in the air in the lungs, by the laws of diffusion, or are other factors active?

At present we cannot produce sufficient reasons for abandoning the view generally adopted, that the entrance of oxygen into the lungs takes place simply by means of diffusion, and further that the amount of oxygen in the blood, within certain limits, does not especially depend on the amount of oxygen in the atmospheric air.

Concerning the elimination of carbonic acid gas in the lungs, we are likewise without reasons for abandoning the generally adopted view according to which the carbonic acid gas coming from the blood enters the lungs simply by the law of diffusion.

It would lead us too far on this occasion to go into details, so that I simply mention these theories in order to show how they have been quoted to explain one of the effects of carbonic acid inflation of the rectum.

Ephraim administered carbonic acid gas by the rectum to a number of patients suffering from chlorosis (more correct would be the word chloriasis) and found that under this treatment the number of red blood-corpuscles increased, and he reasons as follows: The large amount of gas having been introduced into the rectum is quickly absorbed, passes through the veins, enters into the alveoli, and from there, obeying the physical law, is diffused in the upward direction, whereby an excess over the normal process of the diffusion of the gases takes place; that is, more than the normal amount of carbonic acid gas ascends, and more than the normal amount of oxygen descends, the ventilation of the air-passages being thus increased.

Rosenbach's experiments, especially those made on the cadaver, confirm the well-known fact that we cannot, by way of the rectum, inflate the small intestine.

This much about the imaginary dangers of asphyxiation and of the gas passing the ileocecal valve. There is no danger of asphyxiation so long as there is opportunity of elimination of the gas by the lungs.

A few seconds after the gas enters the rectum there is produced

a sensation of warmth, then a slight desire to evacuate the bowel, which immediately passes away. In patients who avoid pressure and control the levator there is no voiding of gas until the bowel is filled to its capacity; but if the patient is unable to control the sphincter sufficiently, we may increase the amount of gas which we introduce; then, while more gas enters than escapes, a satisfactory filling up of the intestine takes place. The abdomen gradually becomes expanded, and when the patient commences to complain of tension the introduction of the gas is discontinued.

The effects of the absorption of large quantities of carbonic acid gas, be it by gas-baths (not necessarily gas-water baths, but dry baths) or inflation of the rectum, on the circulation have been described as follows: *The capillaries and arteries become dilated, the amount of blood in both, as well as the blood pressure in the arteries, is increased, the diastole of the heart becomes more effective.* These are moments of significance for the heart and its work, in so far as the intensity of the peripheral arterial circulation is augmented, the drawing of blood from the veins facilitated, the diastolic filling improved, and the heart muscle is given more time for relief and for preparation for renewed energy.

The local effect of the gas introduced into the rectum in dysentery and ulceration of the rectum in general is twofold. By its anesthetic effect it relieves tenesmus and by its stimulant action on the circulation it is healing. My experience and observations have been published from time to time; the last paper on this subject appeared in the *International Medical Magazine* for October, 1902. Carbonic acid gas inflation of the rectum has in some cases given most excellent results in whooping-cough; it has controlled vomiting in pregnancy. Allow me to refer to my publications on the carbonic acid gas treatment in these affections. To the cases of enteritis membranacea already published, I wish to add one which I saw, by courtesy of Dr. Robert Coleman Kemp, in St. Bartholomew's Clinic of New York, a woman of 35 years, who had been passing mucus from the bowels for seven years. During the last five years she had been under observation. I pass around a specimen of membranous strips she had voided. Here existed as complications hyperchlorhydria and enteroptosia. She was treated for hyperchlorhydria by a diet as suggested for this affection by Dr. Illoway, of New York; for enteroptosia by strapping of the abdomen with

rubber plaster, and for enteritis membranacea by inflation of the rectum with carbonic acid gas. I saw patient on December 20, 1902, and learned that under the combined treatment she improved continually in every direction. From January 2 to January 9, 1903, the day she was dismissed, she had passed no more mucous strips. The time is too limited to enter into details of this case. However, we need no cases to prove the advisability of carbonic acid gas inflation of the rectum in enteritis membranacea; the physiologic effect of the gas suggests this treatment.

I will come now to the main subject to speak on, a new observation which I have made, namely, that a rectal fistula can be cured by means of carbonic acid gas alone.

The first case in which I had the gas current pass through a rectal fistula has been described in the *New York Medical Journal* of January 31, 1903. I may be permitted to recapitulate the essential points from this description, and I shall add the continuation of the history of the case.

CASE I.—A., 34 years of age, gave a history of chronic constipation, hemorrhoids, and had chronic prostatitis and a complete rectal fistula of six months' standing, causing painful defecation and difficulty with micturition. The very first application of the gas, which was passed through the sinus into the rectum, gave most marked relief from the complication of symptoms; after about three applications of gas into the sinus on three consecutive days no more gas entered the rectum—the fistula had closed. The first application of the gas was made on December 30, 1902. On January 12, 1903, the fistula was completely and entirely closed. After this date, at intervals which became more and more prolonged, a minute superficial collection of pus at the slightly reopened external orifice of the fistula would appear, and I applied gas to this little opening for about half a minute. During these last four weeks there has been no more discharge. The details of the treatment were given in the paper quoted. The patient is cured of fistula, the piles have given no more trouble, and there is no more trouble with the prostate.

CASE II.—A second patient came to my office, February 24, 1903, sent by courtesy of Dr. B. S. Booth, of Troy, New York. This was a case of incomplete external secondary tuberculous fistula, with wide orifice and drooping margins forming a cavity

large enough to admit a pea. At the bottom of this cavity was a hole admitting a very small probe. I applied the gas at first once, and later on twice, a day. The walls of the cavity which had presented an ulcerating surface healed soon under this treatment. There was no more drooping of the edges, but the hole at the bottom did not close, and the discharge, although much diminished, did not cease entirely. I finally passed the ligature through the sinus and out through the rectum.

CASE III.—The third case was that of a gentleman, 68 years of age, who had a complete rectal fistula connected with a large abscess cavity, which opened near the left gluteal fold about an inch and a half from the anus. Forty years ago the patient suffered from hemorrhoids which had protruded, the tumor being the size of a fist. Application of cold, however, had been of such good service that they gave him no particular trouble during these last 35 years, except occasionally a slight hemorrhage. During the first three weeks of this year he had been suffering from constipation. At last he had had a large passage of hard lumps, without, however, experiencing any noteworthy pain with this defecation. About February 10 the formation of an abscess was noticed, and this abscess, situated in the left gluteal region, was lanced on February 15, and had kept running ever since. About the middle of March the patient's physician had introduced carbonic acid gas into the cavity of the abscess, and the gas had passed through the sinus into the rectum.

When the patient came to my office, April 19, I suggested to enlarge the opening of the abscess, which opening was in no proportion to the size of the cavity; it was so small, in fact, that it just admitted the nozzle of an ordinary dropper. I found a large amount of thin pus retained in the cavity, which could be emptied by pressure upon the surrounding parts. The patient refused the little operation because he could only remain a few days in New York, and while here had to attend to important business, making it impossible to observe rest during the day.

Introduction of the gas into the cavity of the abscess and through the sinus into the rectum caused no other unpleasantness than that which is always experienced when the bowel is filled with the gas to its utmost capacity. Under daily applications for one week the discharge from the abscess diminished, and after a few days no

gas would enter the rectum, but only fill up the cavity of the abscess, which would pouch out like a balloon. After the cavity had thus been inflated to its capacity, the gas—on withdrawing the nozzle—would escape with a certain amount of power. I am under the impression that if I had had the opportunity to make a free incision, to lay open the cavity, the result would have been prompt cure of abscess and fistula.

CASE IV.—The fourth case was an insignificant, incomplete, external fistula, with the orifice close to the anal margin, the sinus running closely along the rectal wall, so that the probe inserted was separated from the lumen of the bowel only by a thin membrane. The patient had had urethritis eight years ago, and is suffering from chronic prostatitis. The fistula is of two years' standing. Gas application daily continued for one week did not close the fistula nor cure the discharge. The prostate was treated by massage. After I had incised the fistula in the ordinary way, it healed promptly. Two or three days after the incision discharge had ceased completely. Here the sinus did not run through a fleshy part; there was no base from which luxuriant granulations could develop.

To sum up: The application of the gas in one case brought, within a very short time, complete cure of a complete rectal fistula, a cure which otherwise could only have been effected by operation. In the case of tuberculous fistula there has been a partially beneficial effect. In the case of the fistula with abscess the gas has, under the circumstances, been of good service. In the case in which the sinus was close along the rectal wall no closure of the fistula by gas alone was secured.

It may be of interest to those who are not familiar with the history of the treatment of rectal fistula to read the graphic description given by Esmarch: "Hippocrates taught to treat fistula in ano by means of ligature; Galenos and his pupils were opposed to this method and substituted extirpation. The surgeons of the seventeenth century considered the cure of a fistula a very difficult task, because they were of the opinion that such a cure could only be accomplished when all pathological, that is, all indurated, tissue would be completely destroyed. The operation had become a very barbarous one, consisting in extirpation of the fistula, and all the callosities of the rectal wall in its neighborhood, by means of the

actual cautery or some chemical caustics. The consequence was, the patients thus operated on who survived the operation, who did not die in consequence of hemorrhage or pyemia, were either not cured or were left with incontinentia alvi or anal stricture. They were in worse condition than before the operation. The after-treatment was as complicated as the operation itself.

"For this reason, the operation of rectal fistula was much threatened, and the physicians took all possible pains to cure fistula by other means—ointments, baths, and internal remedies, but, as a rule, without success.

"This condition of things explains the fear of Louis XIV, who in the year 1686 was suffering from rectal fistula, and consented to the operation only after all other possible remedies had been tried in vain on many of his subjects suffering from the same evil. He was operated by his first surgeon, Felix, who invented a new knife with which he performed the operation on the king, and which was afterward called the royal knife. The operation, performed November 21, 1687, was a success.

"Dionis, who has reported all details of the case, tells us that afterward many people, not only of the royal court, imagined themselves suffering from the same affliction as their king, in order to have the honor of being cut with a knife which bore the royal name.

"Only after Pott, in 1765, had taught that the callosities need not be destroyed and that a simple incision was sufficient to heal the difficulty, did the operation lose its danger and its horrors. Still, Syme in the year 1854 complains that there existed yet surgeons in England who could not be persuaded to abandon the old method, and that he had seen several cases of frightful destruction, which had been caused by rural surgeons operating for simple rectal fistula."

Again and again have means been tried to cure fistula without operation. None has been successful; but this fact should not deter us from paying attention to the carbonic acid application, which will, according to the few observations related above, effect a radical cure in some cases and will be an excellent adjuvant in all, even in those which have to be or which have been operated.

THE SERUM TREATMENT OF TYPHOID FEVER

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THE demonstration of the usefulness of a remedy can only be made by a strict and prolonged comparison of the results obtained with it as against those furnished by the other habitual methods of treatment.

The question that I wish to treat to-day is, whether the anti-typhoid serum, the mode of preparation of which I have reported elsewhere, has the same preventive and curative effect in assisting man to withstand an attack of typhoid fever that it shows in animals subjected to the action of typhoid virus, and also whether injections of this serum are harmless for man.

Rapid recovery in a few cases, improvement in symptoms, and favorable results in a limited number are not proofs, as the physician may be the victim of mere chance or of a lucky series. Any new treatment must be compared with its predecessors for a long period of time before it can be held to show anything.

I have thought that such a comparison could be made by taking, on the one hand, the data noted on the official registers of all the Paris hospitals concerning the typhoid death-rate during a period of 20 months, and, on the other, the data of the official register of my personal wards during the same period of time. In the Paris hospitals the usual hydrotherapeutic and pharmaceutic treatment is applied; in my wards alone is the antityphoid serum used with hydrotherapeutics. Consequently, during a given period and a given epidemic in the same town the total number of cases in its hospitals act as a test for the results furnished by the treatment in my wards.

In order that there might be no possible mistake, I personally gathered from the official registers of each hospital the figures that I am about to give. I may note, in passing, that for the last three or four years we have had to deal with a typhoid fever of a more serious type than during the years that preceded; the cause of this unaccustomed severity, which reappears in spells in all infectious

diseases, and particularly in diphtheria and typhoid fever, is unknown.

In the 20 months between April 1, 1901, and December 1, 1902, in the 15 leading hospitals of Paris, 1192 patients left the wards cured after having been treated for typhoid fever, and 286 succumbed. From these statistics follow these three conclusions:

(1) The average death-rate from typhoid fever in all the Paris hospitals during this stated period was 19.3 per cent.

(2) The deaths in certain hospitals were in greater number than in others, but in all cases, provided the number of patients were sufficiently large, the average death-rate did not go below 12 per cent.

(3) Average figures based on a small number of cases have no signification. In proof of this I will only give one example, because that one will suffice: in Laënnec Hospital, during the last three trimesters of 1901, 44 cases of typhoid fever were received, and not one of them died; whereas in the following year (1902) the same hospital, receiving patients from the same wards of the city, and with the same medical and nursing staff, had 42 cases with 11 deaths.

In opposition to these figures let us place those given by the official register of my wards for the period mentioned, nearly 21 months: the number of patients treated for typhoid fever was 186, of whom 7 died. The death-rate, therefore, was 3.7 per cent. In this number is not included the case of a young woman who, while convalescing from typhoid fever, contracted, by direct and ascertained contact, a toxic form of diphtheria of the nasal fossæ and throat, which carried her off in 30 hours.

The difference between the figures of the death-rate of the Paris hospitals except mine, and the death-rate of my own patients, is too great to be attributed to chance, and I feel authorized in attributing this saving in human life to the use of the antityphoid serum.

It is true that, in addition to the serum, I, as also my colleagues, use baths, cold or warm, or cold effusions, in treating typhoid fever. Last year the objection was made that the favorable results obtained by the combination of the antityphoid serum and hydrotherapeutics might simply be due to the cold baths. We know the results that have been obtained in the Paris hospitals by the bath treatment, even when most rigorously applied. There are many demonstrative

statistics on this point which show that this method of treatment, which has given and continues to give such invaluable aid, has never with us, provided a sufficiently large number of patients be considered, been able to show a death-rate of less than 12 per cent. The difference between the latter figure and that of 3 or 4 per cent., which I obtain in my wards, appears to me to represent exactly the improvement that can be attributed to the serum.

While it is interesting to know that antityphoid serum therapeutics gives a small death-rate, it will be, perhaps, more interesting still to know the reasons why it failed to act in certain cases. The following are the clinical and anatomic notes concerning the 7 cases that succumbed in my series of 186: First case: A young man brought to the hospital with profuse intestinal hemorrhage; developed lobar pneumonia and died. Second case: A man of 40, brought to the hospital with ataxo-adyamic typhoid fever, suffering besides, from syphilis in the secondary stage and acute gonorrhea; died in three days in spite of the serum. Third case: A young man brought to the hospital in a coma; death in two days. At post-mortem we found the lesions of typhoid fever, as well as generalized purulent peritonitis without any intestinal perforation. Fourth case: A young woman suffering from typhoid fever complained of peritoneal pain; succumbed later to intestinal obstruction due to interadhesion of the loops of the intestines. Fifth, sixth, and seventh cases succumbed to intestinal perforation.

I shall not dwell upon the modifications caused in the evolution of the disease by the injections of serum, as in a previous publication I gave sufficient information on this subject. There is, however, one point that I should like to consider: To what degree does the serum protect the patient against intestinal perforation? To solve this problem, it will be necessary to compare the results given by large and carefully compiled series of cases, as the frequency of perforation varies with the severity of the epidemic. My readers will remember the violent onslaught made against the bath treatment, which was accused of causing intestinal perforation; time has shown the injustice of this accusation. Now, as concerns the frequency of this accident, if we turn to the publications of the authorities on this question, Murchison in England, Griesinger in Germany, and Flint and Osler in America, we find the following figures. Murchison—46 cases of perforation in 1580 cases of typhoid, 3.4

per cent.; Griesinger—14 in 600 cases, 2.3 per cent.; while Flint gives the frequency as 2.74 per cent., and Osler, 2.7 per cent. (23 in 829 cases). In a word, the total given in a large number of cases shows the frequency of intestinal perforation to be about 2.69 per cent. In the 186 cases treated in my wards by the antityphoid serum I had three of fatal perforation, and two others operated on 9 and 10½ hours after the occurrence and who recovered, thanks to the operating surgeon's skill. This makes 5 cases of perforation, and shows that among hospital patients, who only enter the wards when they have already been ill for a week or more, the serum does not appear to diminish the frequency of this terrible complication. The explanation of this fact is that the essential cause of perforation is intestinal necrosis, which necrosis has already taken place at the beginning of the second week. The 5 patients with whom perforation occurred were treated by the serum, 1 on the twelfth day, 3 on the tenth, and 1 on the eighth day.

I have not yet seen a perforation occur in patients treated with the serum at a period nearer the beginning of their illness. In this connection let me call attention to the following. At the navy hospital at Toulon, where the sailors are usually admitted at the very beginning of the disease, the serum has been used in 151 cases of typhoid fever, among whom perforation occurred only once, and even then in the case of a man whose treatment was not begun until the eighth day. This shows the great desirability of injecting the serum as near the beginning of the disease as possible. By acting promptly I have succeeded in aborting in five or six days' time perfectly certain cases of typhoid fever. The objection will be made that so much hurry exposes the operator to injecting serum in cases that are not typhoid fever at all. My reply is that this makes very little difference, as a small dose (2 c.c.) of serum administered to a man, either in good health or suffering from some disease other than typhoid fever, has no evil consequences.

The number of patients treated in my wards is too small to enable anyone who has not followed the evolution of the fever to form an opinion; to settle finally the true value of the serum, we shall require several thousand cases. Still, limiting ourselves to hospital cases, the number of patients systematically treated already exceeds 500. To the 186 cases of the present statistics can be added the 70 cases previously reported by me, with 4 deaths, and

the 100 cases of the statistics for last year, with 6 deaths, making a total for my wards of 356, with 17 deaths, a death-rate of 4.7 per hundred. I may add that the death-rate of the present year has been lower almost by half than that of the previous years, because I have learned better how to handle the serum.

On learning of the results obtained in Paris, the director of the Navy Health Board at Toulon authorized the use of this serum among the sailors treated for typhoid fever; and in the Navy Hospital, between August 10, 1902, and the end of November, 151 cases were so treated, of whom 13 died. The result, although favorable in itself, was less so than in Paris, because, in spite of the competence of the physicians in charge, they naturally did not have much experience in the use of this new remedy, and because the bath treatment, which I also apply in my wards, could not be thoroughly carried out. This makes a total of 507 cases of typhoid treated in adults in hospitals by the serum, cases that could be carefully followed in detail, and that have given 30 deaths, or a total death-rate less than 6 per cent.

If we compare these figures with the results that we are accustomed to consider as the very best, those of the German army, which last year showed a death-rate of about 9.5 per cent. (87 deaths in 929 cases), we see that the death-rate of cases treated by the serum is considerably less than that given by the usual methods of treatment. Among children the results are equally favorable, and one of my colleagues—physician to a children's hospital—intends to make them public before long.

One of the clearest proofs of the action of the serum on the lesions of typhoid fever is the way in which it heals up certain local manifestations, such as osteitis and periostitis, occurring during convalescence of the disease, and sometimes giving rise to interminable suppuration. I have on several occasions cured in a very short time, under the influence of the local injection of one or two drops of serum repeated every two weeks, cases of inflammatory osteoperiostitis with hyperostosis that had suppurated for years.

I am very willing to admit that the 507 cases of typhoid fever in adults treated with serum in hospitals do not supply the elements for a final judgment as to the exact value of the remedy. To prove this point definitely, we should require many cases and years of observation.

If we expect to make any great diminution in the typhoid mor-

tality in Paris hospitals, we shall have to make an effort to carry through some reforms, to which I take the liberty of calling attention. Anyone who has taken care of many typhoid fever patients knows the extreme importance of skilful and constant nursing in the patients' chance of recovery. These patients require not only a staff of nurses that are devoted, but that have, as well, special skill, and that, so far as possible, are already possessed of immunity, as interns and nurses frequently contract the disorder. Patients who have never had typhoid fever, and who come into the hospital for some other complaint and are placed in the next bed to a typhoid case, are also liable to take the disease. How many cases have we not all seen similar to the one that was recently reported to the Academy of Medicine by Albert Robin, in which a young woman, who entering his wards for some simple disorder was placed by the side of a patient suffering from typhoid, took the disease and died. We must therefore have in Paris one or more hospital services given up to typhoid fever, where the wards will be supplied with all the necessary outfit, and to which must be attached a surgeon who at the first call will operate on cases of intestinal perforation, and save many patients whom the delay of a few hours inevitably condemns to death.

I wish, now, to speak of the experimental results noted in animals subjected to the action of the typhoid-fever virus and treated by the antityphoid serum; they throw a strong light on antityphoid serum therapeutics, as well as on its mechanism.

It is necessary to consider separately the condition of infection produced by the bacillus and the intoxication caused by the soluble toxin secreted by this microbe. If beneath the skin of the ears of several rabbits, some of them untouched, and others treated a few hours previously with 2 or 3 c.c. of serum, we inject a similar dose of typhoid bacilli, we find, in five or six hours' time, that in the ears of the untouched rabbits the microbes swarm and develop rapidly as they would in a culture medium, whereas in the ears of the rabbits treated with serum the immense majority of the bacilli are absorbed by the phagocytes and rapidly destroyed. The preventive injection of the serum is therefore an anti-infectious form of treatment.

It is, in addition, an antitoxic treatment, for if we inject beneath the skin of an untouched rabbit a quantity of soluble typhoid toxin that is somewhat less than a fatal dose, in a few hours we will

see that a considerable loss of flesh has taken place, and in the blood we can detect the disappearance of a very great number of leukocytes, particularly the polynuclear ones. But, little by little, the animal will recover; abundant crops of polynuclear leukocytes will appear in the blood, and the animal will regain its weight. Its vitality, however, will bear witness to the attack for some time, its coat will be dull, and its hair will fall out in spots, while its appearance will not be flourishing. If, on the other hand, we make in another animal the same injection of toxin, but first taking the precaution of injecting beneath the skin, 2 to 24 hours previously, a cubic centimeter of serum, the animal will hardly be ill, will only lose a little weight, and the destruction of leukocytes will be unimportant. The blood of a rabbit treated preventively by the serum acts, when under the influence of the toxin, like the blood of a rabbit that has been rendered immune by small and repeated doses of toxin. By means of this injection of serum the animal has acquired the power of supporting, without succumbing, twice the amount of poison that would kill another animal in 36 hours.

When the serum and toxin are injected at the same time, but separately, the effect of the latter on the blood is found to be almost as violent as if it had been injected alone; but the defensive action of the leukocytes is more rapid and intense than in animals who have not been treated by the serum. The polynuclear leukocytes, in particular, reappear in the blood more rapidly and in greater number.

If the injection of serum is made too late after the beginning of the intoxication, and if the latter is severe, the favorable action is inhibited, as it were, and does not take place. Finally, the effect of the serum injection lasts for some time; animals whose injection of serum goes back six or seven days, still show great power of resistance against the injections of toxin. From these facts follow the indication to inject the serum as early in an attack as possible, and not to repeat the dose frequently.

In order really to understand the mechanism of this serotherapeutic action, we must examine the spleen and bone marrow of the animals experimented with. The difference between the organs of treated and untreated animals is so great that it is striking, in sections, even to the naked eye. The spleen and bone marrow of rabbits which have only been injected with the toxin show in a few hours a condition of intense congestion; the lymphoid apparatus of the spleen, and the medullary tissue, are manifestly undergoing

slight but laboring reaction. On the other hand, the spleen and bone marrow of animals into which both the serum and toxin have been injected are equally swollen, but this condition is not caused by congestion; it depends on enormous hypertrophic reaction of the lymphoid and myeloid tissue. The splenic corpuscles are increased in size and laden with lymphatic cells. The medullary tissue shows signs of active recuperation; the fat is absorbed and the frame-work is filled with a large number of young cells with usually basophilic protoplasm.

In a word, this experimental study teaches us that the antityphoid serum acts on the living virus so as to make it more susceptible to the attack of the cells, and also on the toxin, which it helps to destroy. It also acts indirectly by intensifying the activity of the phagocytes and of the organs by which they are generated. Its full effect can be counted on when the lymphoid and myeloid apparatus are not profoundly poisoned, and are capable of reacting to its effect. For this reason the serum is specially active at the beginning of the disease, and this is also why, when there is severe intoxication that has already lasted for some time, this power of reaction must be handled with care, so as not to risk checking it altogether, and relatively small doses of serum must be given.

This is the essential point in the application of the antityphoid serum, which application will always require in the physician a thorough clinical knowledge of the disease and a special study of the remedy. The general rule is that the more severe the case the smaller must be the dose of the remedy. When there are serious nervous symptoms, or when the case has been running for some time, rapid recovery must not be sought after, but a small dose should first be given to increase the patient's strength of resistance and enable him to get past the dangerous period.

This serum treatment, which is strictly specific for typhoid fever through stimulation of the phagocytes, can be most satisfactorily combined with the bathing treatment. These two methods used together are not antagonistic in any way, but each seems to increase the other's efficacy through their collaboration. As to the results that we owe to them, I have already said that the strictest application of the bath treatment in our hospitals, if we only take the most favorable statistics, gives a death-rate of 12 to 13 per cent.; through the addition to the treatment of the antityphoid serum I think that this death-rate ought not to exceed a maximum of 4 to 5 per cent.

Medicine

MALARIAL INFECTIONS: THEIR PARASITOLOGY, SYMPTOMATOLOGY, DIAGNOSIS, AND TREATMENT ¹

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By the term "malarial infections" we mean certain febrile diseases due to the invasion of the blood by parasitic animal organisms known as plasmodia malarix. The term "malaria," meaning bad air, comes to us sanctioned by years of usage, and arose from the supposed connection of bad air with the disease. In the light of our present knowledge this name is erroneous, as we now know that the air of swamps and of so-called malarious districts has nothing whatever to do with the origin of the malarial infection. As the name, however, has become fixed in our medical nomenclature, it would probably be unwise to attempt to change it.

The name "plasmodia," applied to the parasites causing malarial infections, is also far from being correct, and that suggested by Welch, of "hæmamœbæ," would be preferable. The same difficulty exists here, however, as in the name "malaria," in that the use of the term "plasmodia" has become so common and is so well understood by the medical profession that a change is probably not advisable.

¹ The observations noted in this paper are derived from the study of over 3000 cases of malarial fever in which the parasites were demonstrated in the blood. I am indebted to the Surgeon-General of the Army for permission to use the data collected, and to William Wood & Co., of New York, for the use of data from my work upon "Estivo-autumnal (Remittent) Malarial Fevers."

In the following necessarily brief *resumé* of malarial infections I shall discuss the parasitology, symptomatology, diagnosis, and treatment of these diseases, giving the facts which seem to me to be the most useful to the general practitioner. It is exceedingly difficult to condense into a short article a subject so large that numerous extensive volumes have been written upon it, and I hope that any omissions which may seem to some to be of interest or importance will be pardoned on this account.

PARASITOLOGY OF MALARIAL INFECTIONS

All authorities of the present day concur in dividing the parasites of malaria into three distinct classes: the tertian, the quartan, and the estivo-autumnal parasites or plasmodia. Most of the Italian authorities, together with many other authorities who have studied malaria in the tropics, have made a subdivision of the estivo-autumnal parasite into two varieties: the quotidian and the tertian. This subdivision is concurred in by the writer and will be followed in descriptions of the parasites in this contribution.

All varieties of the malarial parasite are found within the red blood-corpuscles in the human body, and are essentially parasites living upon and within these cells. In this situation they destroy the red corpuscles, and produce the well-known anemia peculiar to malarial fever, together with the pigmentation due to the destruction of the hemoglobin of the red cell.

In describing the parasites of malarial fever in the light of our present knowledge, two life cycles must be considered: (1) The human cycle, or that occurring within the infected patient; and (2) the mosquito cycle, or that occurring within the infected mosquito.

THE TERTIAN PARASITE.—*Human Cycle.*—The tertian parasite appears first within the red cell as a small, actively ameboid, hyaline body of various shapes, according to the rapidity and the extent of the ameboid movement. The outline of the organism is not very distinct at first, but as it grows older and pigmented it becomes more distinct. This hyaline stage is quickly followed by the appearance of a few minute granules of reddish-brown pigment situated within the hyaline parasite, and showing active movement. At first the parasite occupies but a minute portion of the red cell, but as it continues to grow, more and more of the red cell is occu-

pied by it, until when full-grown the entire cell is filled. The growth of the parasite takes place gradually, covering a period of 48 hours. The full-grown parasites have a rather distinct outline, are possessed of active ameboid movement, the pigment showing very active motion, the red cell containing the parasite being swollen in appearance and much paler in color than the normal cells surrounding it. Toward the end of 36 hours the parasite has approached to nearly its full growth, only a narrow rim of the infected red cell showing around it. Ameboid motion has become almost entirely lost, the parasite being circular in shape, well defined, the pigment rapidly motile, very much increased in quantity, still, however, finely granular in appearance and reddish-brown in color. The red cell containing the organism is greatly increased in size, being as a rule twice as large as the normal uninfected cell. At the end of 48 hours, so-called segmentation occurs. The pigment becomes collected at the center or at one side of the parasite in the form of a close clump, and fine radial divisions are noticed branching from this center dividing the parasite into segments. As a rule, there are two rows of segments,—one row surrounding the center, another surrounding the first row, but very often the segments are irregularly arranged and are always devoid of pigment. The segments vary in number from 12 to 24, the mean average being about 16. At this time the containing red cell has apparently disappeared, being entirely destroyed by the invading parasite, and the segments are finally liberated in the blood-plasma. In the human cycle of the parasite these segments again infect red blood-corpuscles, and the life cycle continues as described. A certain proportion of the parasites do not undergo segmentation, and are intended to complete the life cycle of the organism in the mosquito, which will be described later. The tertian parasite completes its human life cycle in 48 hours. (See Fig. 1, Frontispiece.)

THE QUARTAN PARASITE.—*Human Cycle*.—The quartan malarial parasite at first appears, as does the tertian, as a small, actively ameboid, hyaline body, without pigment, within the red corpuscle, but it is less motile than is the tertian. It rapidly becomes pigmented, the pigment being in the form of larger granules than in the tertian and less motile, the outline of the parasite being much more distinct. Instead of the swollen, pale-red cell seen in the tertian infection, the infected red cell in quartan fever is normal

in size, or perhaps slightly below normal, and darker green in color instead of pale. This serves at once to distinguish the two varieties upon microscopic examination of the blood. The parasite slowly increases in size, and in doing so becomes less ameboid. More pigment is noticed within the parasite, this pigment being, as a rule, collected around the edge instead of being diffused widely throughout the protoplasm, as in the tertian variety. The pigment also, as the parasite enlarges, becomes almost motionless, and when the parasite is full-grown, entirely so. The granules of pigment are considerably larger than in the tertian, more black in color, and do not collect in small clumps within the parasite. As growth increases, the parasite tends more and more to fill the infected red cell, and when full-grown,—that is, at the end of 72 hours,—it almost entirely fills the cell, a small greenish rim of hemoglobin still being visible around the organism. When full-grown the parasite is very distinctly outlined, being much more refractive than is the tertian variety, the pigment absolutely motionless and collected around the edge, the shape circular, and ameboid motion entirely lost. At the end of 72 hours segmentation occurs, as it does in the tertian variety, the pigment becoming collected at the center or in a star-like arrangement distributed from the center; radial striations appear, dividing the organism into from 8 to 12 segments. These segments are more distinctly outlined than are the tertian. The segments are generally arranged in a perfectly symmetrical manner around the central pigment, giving the so-called “daisy” or “marguerite” appearance to the parasite at this stage. When segmentation takes place, each segment becomes free in the blood-plasma, and again, in the human life cycle, infects the red corpuscle, the same process being repeated. As in the tertian, however, certain parasites do not undergo segmentation, and these are the ones intended to carry on the life cycle of the organism within the mosquito. The human life cycle of this parasite is completed in 72 hours.

ESTIVO-AUTUMNAL PARASITE.—*Quotidian Form, Human Cycle.*

—As stated at the beginning of this contribution, I believe that there are two distinct varieties of the estivo-autumnal parasite: the quotidian and the tertian. These are distinguishable microscopically, and the symptoms produced by them are easily distinguished clinically. The quotidian parasite appears first in the infected red cell as a very minute ring-shaped or round hyaline body, which

upon close inspection shows very active ameboid motion. The outline of the organism at first is indistinct, but gradually becomes more distinct and refractive. The round forms are perfectly hyaline in appearance; the ring-form, however, consists of a narrow hyaline band enclosing a small islet, showing the normal greenish-yellow color of the infected corpuscle. Most authorities believe that this appearance is due to the fact that the center of the parasite is much thinner than is the edge, thus allowing the normal color of the corpuscle to show through. In my opinion, however, this is an erroneous conclusion, as careful observation of these ring-forms will show that they often become perfectly hyaline, and in so doing the protoplasm of the organism flows in from the edge of the ring, thus tending to prove that no protoplasm existed in this greenish-colored area. The ameboid motion is very active, and can only be distinguished by very careful observation, on account of its slowness of extent and rapidity of motion. The corpuscle containing the parasite is generally smaller in size than the normal corpuscle, and dark green in color. It is very apt to become crenated and vacuolated. Double infections, or even triple infections of the corpuscle, are apt to occur in this type of the parasite. This is the form of the parasite most commonly observed in the peripheral blood. A certain number of the organisms become pigmented, the pigmentation consisting of a small, generally solid block almost black in color, situated at some portion of the edge of the parasite or at the center. This pigment is not motile. In rare instances this pigment consists of fine granules, but never numbering more than three or four.

The pigmented stage is quite often observed in the peripheral blood. Segmentation occurs at the end of 24 hours, little change being noticed just prior to segmentation in the parasite. The parasite, when full-grown, that is, just before segmentation, is never more than one-fourth the size of the red blood-corpuscle, thus distinguishing it at once from the quartan and tertian varieties, which fill the corpuscle. At the time of segmentation, the pigment is collected at the center of the parasite, and faint radial striations can be detected starting from the center and dividing it into from 6 to 8 very minute round or oval segments. A peculiarity of the segmenting stage in this form of parasite is that it occurs plainly within the red blood-corpuscle. The segments when liberated in

the blood-plasma in the human cycle again infect the red cells, and the same process is repeated. The human life cycle of this variety is completed within 24 hours.

ESTIVO-AUTUMNAL PARASITE.—*Tertian Form, Human Cycle.*
—Like the quotidian, the tertian estivo-autumnal parasite appears first within the infected red cell as a round, hyaline ring or disk. The following differences are to be noted: The ring is larger, being from one-fourth to one-third the size of the corpuscle; it is irregular in outline, one portion of the ring being larger than the rest; it is highly refractive and very sharply cut, looking as though it had been cut into the corpuscle with a punch. Upon observation, distinct ameboid motion is noted, not as rapid as in the quotidian parasite, and the ring form often changes to a clear hyaline disk. Only very rarely is more than a single parasite seen within one corpuscle. The infected corpuscle is greenish in color, smaller than the normal corpuscles surrounding it, and is apt to be crenated. In the course of from 20 to 24 hours the hyaline ring-form or disk becomes pigmented, the pigment occurring in the form of very fine reddish-brown granules, somewhat resembling those observed in the benign tertian variety. The pigment is present in larger amount than in the quotidian parasite and is motile.

As the growth increases, the ameboid motion is lost, as is also the ring-form, and at the time of segmentation the organism occupies about one-half of the infected red cell. Segmentation occurs at the end of 48 hours, the parasite at this time being at most not more than one-half as large as the red cell, and the pigment being collected at the center. Distinct radial striations start from this point and divide the organism into 10 or 15, sometimes even more, segments. At this stage the parasite is very distinct, and the segmentation is much more apt to occur apparently outside of the red cell than in the quotidian. The young segments in the human cycle infect normal red cells, and the process is thus repeated.

THE MOSQUITO CYCLE OF THE MALARIAL PARASITES.—From the pioneer observations of Ross, since confirmed by numerous investigators, it has been established that the malarial fevers are transmitted probably entirely by mosquitoes. These mosquitoes, so far as is at present known, all belong to the genus *Anopheles*. As the mosquito cycles of both the tertian and quartan parasites are the same, they will be described together.

As already noted, certain of the full-grown tertian and quartan parasites do not segment, but instead it will be noticed that the blood contains two distinct bodies, one showing flagella, the other devoid of them. The flagellated parasite occurs in the blood after it has been drawn some time from the body, and is essentially the full-grown parasite in which, after very active movement of the pigment, minute protoplasmic prolongations are sent out from its interior. These are known as flagella. After such flagellation has occurred, the pigment becomes motionless, and the parasite either fragments (or, in other words, degenerates), or else the flagella are liberated and swim off actively through the blood.

The other body, which has just been mentioned and which does not show flagella, is generally perfectly circular in shape, the pigment very sluggishly motile, and generally collected in small clumps around its edge. These bodies, which I have termed the "passive flagellated parasites," will be noticed at times to have flagella attached to them, but never to extrude flagella. According to the observations of McCallum, the explanation of this phenomenon is this: The flagella arising from the flagellated organisms, and which have become liberated in the blood-current, swim around actively in this current until they come in contact with one of the bodies just described (or the passive flagellated body), when one of the flagella penetrates it just as the spermatozoön does the ovum, and this passive body thus becomes fertilized. This process has been found to occur within the middle intestine of the mosquito, the parasites being present in the blood which has been obtained by the insect from man.

The Mosquito Cycle of the Estivo-autumnal Parasites.—In the blood of patients suffering from estivo-autumnal fever, both quotidian and tertian, peculiar bodies are found which are known as crescents, from their shape. These bodies are intended to continue the life of the estivo-autumnal parasites within the mosquito. As mentioned, they are crescentic in form, longer than the diameter of the red blood-corpuscle, and are always developed within the red cells. They have a very refractive, more or less granular protoplasm, and contain within them, generally at the center, sometimes at the extremities, a clump of pigment, usually in the form of minute slender rods or round dots. The border of the crescent is very sharply cut, and, in the quotidian form especially, presents a double outline, due to the enveloping so-called capsule, formed by

the infected red cell which has folded over it. In most crescents a slender hyaline membrane can be detected connecting the two extremities, which is also a portion of the infected red cell. To this portion has been given the name of "bib."

Most crescents present a greenish tinge at the edge, due to the hemoglobin of the red cell, which has retracted about them.

The chief points of distinction between the quotidian and tertian crescents are the following: The tertian crescent is longer, more slender, with pointed extremities, is very refractive, and seldom shows a double outline. The quotidian crescent is short and plump, and is sometimes very small, the extremities are never pointed, but are round, and it always presents a distinct double outline; the protoplasm is less granular and the pigment smaller in amount.

Certain degenerative changes are found in the crescents, consisting chiefly of vacuolization and fragmentation. Such crescents always remain sterile. Occurring with the crescents are the so-called ovoid and fusiform bodies which are developed from the crescents. Crescents are observed in human blood only after an estivo-autumnal infection has lasted some time.

After reaching the middle intestine of the mosquito the crescents undergo the following changes: The crescentic form is lost, a spherical shape being substituted; the pigment becomes active and a certain proportion of the crescents flagellate in a manner similar to the tertian and quartan parasites. Along with the flagellated parasites are observed smaller, perfectly round bodies, with the pigment arranged in a wreath at the periphery, which correspond to the parasites in tertian and quartan fever which do not become flagellated. The flagella are liberated from the parent body just as they are in the tertian and quartan infections, and penetrate these smaller round bodies, fertilizing them.

The process of flagellation just observed in the crescents is often seen in blood under the microscope which has been withdrawn from the body for a short period of time, but actually occurs normally only in the mosquito.

As the various phases of the life cycle of the malarial parasites are the same in the mosquito for all varieties, they will be described together.

Life Cycle in the Mosquito.—As before mentioned, the only species of mosquito which have so far been determined as trans-

mitting malaria, belong to the genus *Anopheles*. Several varieties of *Anopheles* have been found to transmit the disease, the chief one in this country being the *Anopheles maculipennis*.

The forms of the parasites which give rise to the flagellated and non-flagellated bodies have been named by biologists "*gametes*." The male elements of the active flagellated bodies are known as *microgametocytes*, the flagella as *microgametes*, while the bodies which generally become flagellated and which are fertilized by the *microgametes* are known as *macrogametes*.

If a mosquito has sucked the blood of a patient suffering from either tertian, quartan, or estivo-autumnal malaria, this blood containing in the tertian and quartan forms the parasites which become flagellated, and in the estivo-autumnal form the crescents, and if the middle intestine of the mosquito be examined, about 40 hours after the insect has imbibed this blood, spindle-shaped bodies will be found arranged along the intestinal wall. In the tertian and the quartan forms these bodies are spheroidal in shape. They contain considerable pigment, but the pigment, instead of being arranged in a clump, or scattered throughout the parasites, is arranged around the periphery. These bodies are situated on the outer side of the epithelium and the basement membrane of the intestine between the adipose tissue and the muscular wall,—that is to say, they are within the intestinal coats. Examined on the third or fourth day, it will be seen that these bodies have increased in size, that the protoplasm is granular and arranged in a reticulum, that the pigment is less in amount, and that the entire parasite is enclosed in a well-defined capsule. On the fifth day the parasites have increased very greatly in size, and project from the intestinal wall. Within them are numerous minute bodies which are in reality nuclei. Besides these there are numerous refractive bodies which resemble fat. The capsule is very distinct. About the seventh day, the capsulated parasite will be found filled with very delicate filaments, having thin extremities, each containing at its center a small amount of granular chromatin. These filaments measure about 14 microns in length, and are arranged about a center in a ray-like formation. They are known as *sporozoites*.

If the intestine be examined after the seventh day, it will be found that the capsule has ruptured and the sporozoites have thus been set free, the remains of the capsule being distinct and surrounded by them.

If now the tubules of the salivary glands of the mosquito be examined, they will be found crowded with these sporozoites, and it is at this time that in biting a man the mosquito inoculates him with malaria. The sporozoites are forced through the proboscis of the mosquito into the wound, and, after undergoing changes in the human blood which have not yet been determined they appear within the red corpuscles as the small hyaline parasites.

Besides the sporozoites, there are contained within the encapsulated parasites peculiar dark-brown bodies which vary in size and shape. These are considered to be degenerative bodies.

The life cycle of the malarial parasites then may be summed up as follows: (1) The human cycle, consisting of sporozoite, hyaline ameboid body, pigmented body, segmenting body, and, in the estivo-autumnal parasites, the crescent; and (2) the mosquito cycle, consisting of the crescentic body in the estivo-autumnal parasites, and the flagellated and non-flagellated bodies in the tertian and the quartan, the encapsulated parasites, and the sporozoites. (Fig. 2.)

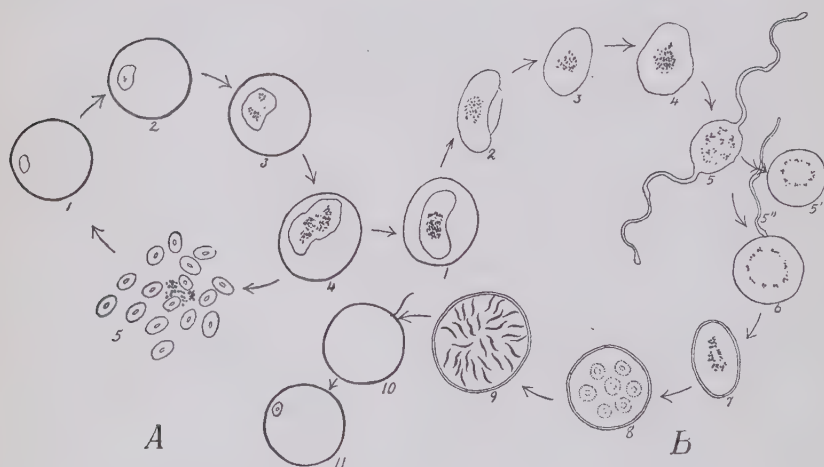


FIG. 2.—Diagram illustrating the human and the mosquito cycles of the estivo-autumnal malarial parasite. A, human cycle—1 to 5; B, mosquito cycle—1 to 11; 2, gamete; 5, microgametocyte; 5', 6, macrogametocyte; 5'', microgamete; 7, 8, 9, encapsulated bodies, the larger filled with sporozoites; 10, blood-corpuscle and sporozoite; 11, young parasite, which goes through the cycle shown in A.

It may be stated that experiments have been made showing conclusively that the mosquito transmits all varieties of malaria to man in the manner described.

STRUCTURE OF MALARIAL PARASITES.—Only in stained speci-

mens can the minute structure of malarial parasites be satisfactorily distinguished. It may be said, in general, that the stained specimens show, in all stages, a protoplasm containing a nucleus and a small dot of chromatin. This structure is easily distinguished in the young parasites, but when full-grown it is often difficult to distinguish the chromatin granules. For a long time it was supposed that the flagellated parasites were degenerative bodies, but the discovery that in stained specimens flagella show a minute thread of chromatin within them, proves conclusively that they are not degenerated.

SYMPTOMATOLOGY OF MALARIAL INFECTIONS

In considering the symptomatology of the malarial infections I shall divide the subject into the following headings: Tertian infection, quartan infection, and estivo-autumnal infection.

TERTIAN INFECTION.—The tertian infection is characterized by a paroxysm, occurring every 48 hours, which may be divided into three stages: chill, fever, and sweat. After a period of a few days of general malaise the patient is generally seized with a severe chill. Although he feels extremely cold during the chill, the temperature continues to rise, and at the acme of the chill has reached to 103°, 104°, or even 106° F. The chill is immediately followed by a pronounced sense of heat, and in a little while the patient will complain as bitterly of this as he previously complained of the sense of cold. During the stage of fever, delirium is often present, and the patient always complains of very severe headache, and there is sometimes muscular twitching. During the onset of the chill, nausea and vomiting are common, but as a rule they do not persist during the stage of fever. After the fever has persisted for a few hours, it rapidly declines to normal, and is accompanied by very severe sweating, the entire skin being bedewed with moisture, often so pronounced that the bed-clothing is saturated. (Fig. 3.)

Grave symptoms, as a rule, are not present, although pernicious types of the benign tertian have occurred.

The Cold Stage.—As has been mentioned, there are generally some prodromal symptoms of an approaching malarial chill, as evidenced by yawning and a general sense of discomfort, headache, and often nausea and vomiting. The feeling of cold commences, as a rule, at the feet, progressing gradually upward. Often it

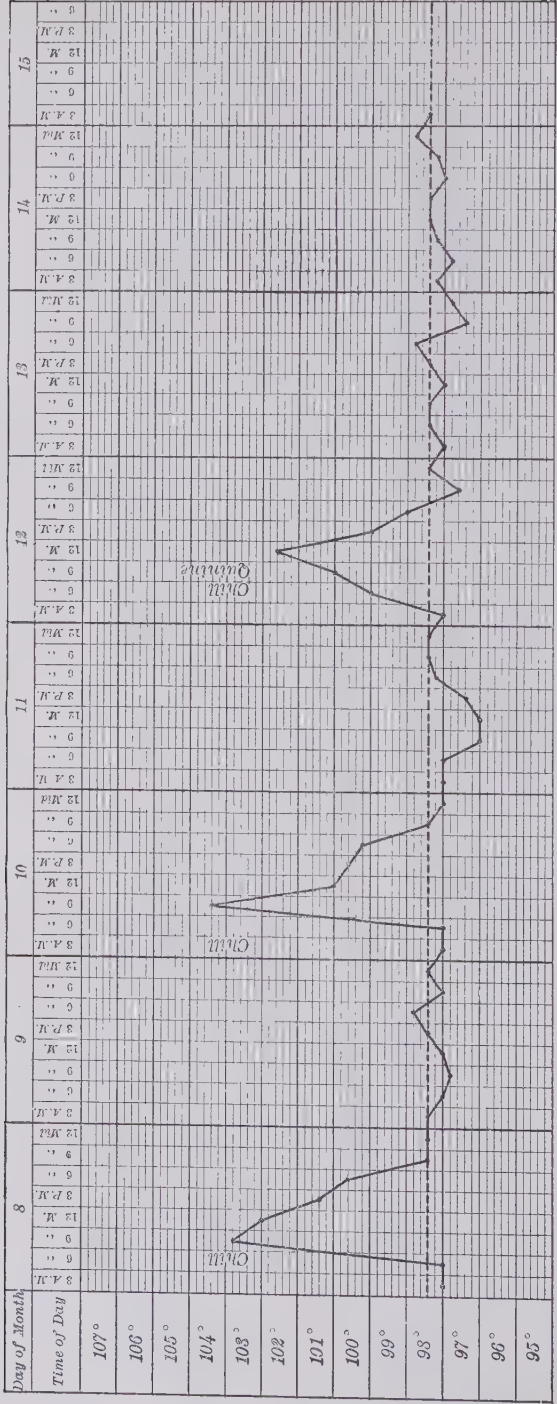


Fig. 3.—Temperature curve in tertian malarial fever.

commences in the back. The chill is, as a rule, severe, the patient shaking vigorously. It is not so severe, however, as in the quartan infection. Sometimes, in mild tertian attacks, the chill may be almost entirely absent, the patient complaining only of chilly sensations running along the spinal column. If, however, these attacks are allowed to continue, a well-pronounced chill will develop during one of the succeeding attacks. The facial appearance of the patient during the chill is one of cyanosis, the lips being blue and the skin bluish-red in color; the extremities are cyanotic, and the skin raised in the well-known condition characterized as "goose-flesh." The pulse is rapid, generally rather weak, and often irregular; the respirations are panting in character. Headache is often very intense. During the chill the temperature rises very rapidly, but it will generally be found that it has begun to rise before the onset of the chill. The duration of this stage varies from one-fourth of an hour to an hour in the most severe cases.

The Hot Stage.—At the commencement of the hot stage the patient complains of flushings of heat, which are rapidly succeeded by sensations of cold. Soon the sensations of cold are entirely lost, and the patient complains bitterly of the intense heat, occasioned by his high temperature. The skin is hot and dry. The patient's facial appearance is that of congestion, the conjunctiva being inflamed and the face red; the respirations are rapid and hurried, the pulse full, bounding, and often dicrotic. These symptoms are often accompanied by more or less cough, showing the presence of congestion in the lungs. During this stage, in the milder tertians, there are no nervous symptoms, but in the severe cases there may be marked delirium or a drowsy condition verging into a semi-coma. This condition is almost always present in those rare cases of tertian infection which become pernicious.

The chief thing complained of by the patient during the hot stage is the severe headache and the intense heat. During this stage the temperature reaches its extreme height, and is often accompanied by marked undulations covering a degree or more.

It is not uncommon during the hot stage to observe cutaneous eruptions, which sometimes lead to a suspicion of some eruptive disease being the cause of the chill. The eruptions, as a rule, are erythematous in character, and often markedly resemble the eruption of measles. Urticaria is a common symptom, especially during

this stage. Herpes is very common, occurring, as a rule, on the lips. I have seen several cases in which herpes of the penis occurred during the hot stage of a malarial paroxysm. The duration of this stage varies from 4 to 6 hours or more.

The Sweating Stage.—As the fever begins to decline, it will be noticed that perspiration appears first on the forehead and face, and the patient at once begins to feel better, and the more severe the sweating, the more rapidly do the unpleasant symptoms accompanying the paroxysm clear up.

Commencing, as has been said, on the face, the perspiration rapidly involves the entire body, and is often so severe that water may be seen trickling from the skin of the arms, thighs, and legs. This stage lasts, as a rule, for from two to three hours, at the end of which time the temperature has reached normal, more commonly the subnormal point.

The decline of temperature is accompanied by considerable weakness of the circulation, as evidenced by a slow pulse of but little strength. In rare cases this stage is accompanied by collapse, and in a pernicious case of tertian infection observed by me this collapse proved fatal.

During the cold stage an excessive amount of urine is often voided, polyuria being a most frequent symptom.

The average duration of the tertian paroxysm is from 12 to 14 hours, but it must be remembered that there are paroxysms so slight as hardly to be recognized, while, on the other hand, paroxysms are observed which cover 24 hours. These, however, are rare.

Physical examination of the patient will generally show an enlarged spleen; but this sign of malaria cannot be relied upon, except in those cases which have severe and repeated infections.

QUARTAN INFECTION.—The symptoms accompanying a quartan paroxysm are exactly similar to those of a tertian, save that they are, as a rule, more severe in character and are more apt to become pernicious. It should be remembered, also, that the quartan paroxysm occurs every 72, instead of every 48, hours. The nervous symptoms, as a rule, are very much more pronounced, headache being more severe, and slight delirium being almost always present. The paroxysm is divided, as in the tertian, into three well-marked periods, and covers a shorter period of time, generally not more than ten hours. (Fig. 4.)

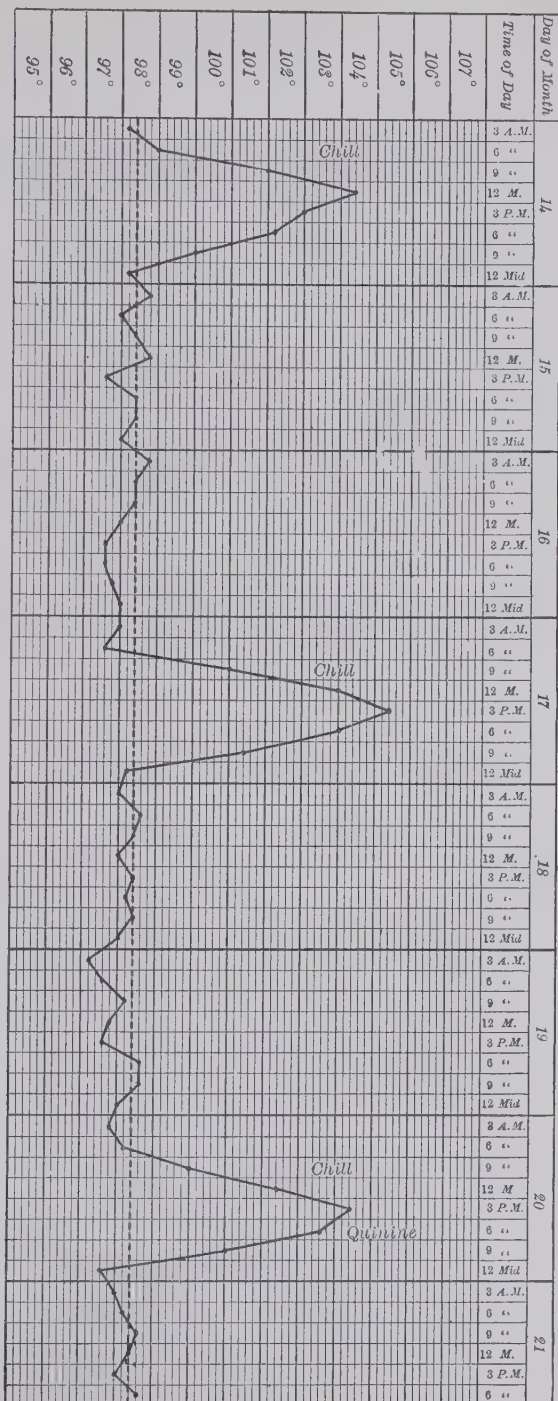


Fig. 4.—Temperature curve in quartan malarial fever.

ESTIVO-AUTUMNAL INFECTIONS.—In considering the symptomatology of the estivo-autumnal infections, it is necessary to describe each variety separately.

Clinically, all estivo-autumnal infections should be classed as severe infections, in contradistinction to the quartan and tertian, which are usually considered as mild infections. It should be thoroughly understood, however, that a quartan or tertian infection can become pernicious, although pernicious cases are much more common in the estivo-autumnal varieties. The old idea that there is a parasite peculiar to the pernicious infections has been exploded, and it is now recognized that any malarial infection may become pernicious and that the parasites accompanying such infections do not differ in any respect from those accompanying the mildest infections.

The estivo-autumnal types of malaria occur most frequently in tropical or subtropical countries, but are by no means rare in the temperate regions. In the latter they occur generally during the months of July, August, September, and October, hence the name "estivo-autumnal." In the tropics, however, they persist throughout the year, and are not characterized by any marked seasonal prevalence.

As I have stated, I believe that the estivo-autumnal infections are caused by two distinct parasites, one completing its cycle of development in the human body in 24 hours, the other in 48 hours. Either of these parasites is capable of causing pernicious infections, and from my own observations I believe that the tertian parasite is most commonly concerned.

As to the frequency of the occurrence of the two types, there can be no doubt that the tertian is altogether the most common. From the data which I have collected, embracing nearly 2000 cases of estivo-autumnal fever, in which the parasites were observed in the blood, 75 per cent. were due to the tertian variety.

The following two points I would specially emphasize in considering the symptomatology of the estivo-autumnal infections: (1) That there is always an element of danger present in these infections, as they may at any time become pernicious; and (2) that the impression which formerly prevailed that these fevers are accompanied necessarily by a remittent temperature curve is entirely

false, as these fevers, if uncomplicated, are just as regular in their manifestations as either the simple tertian or quartan fevers.

No one can deny that irregularities of temperature are more common in the estivo-autumnal infections, but too much stress has been laid upon this point. Any malarial fever may become irregular; and this is especially true of cases which have been unscientifically treated with quinin.

From a clinical point of view, the estivo-autumnal infections may be divided as follows: (1) The tertian estivo-autumnal fever, (2) the quotidian estivo-autumnal fever, (3) the pernicious estivo-autumnal fever, and (4) the latent and masked estivo-autumnal fevers.

THE TERTIAN ESTIVO-AUTUMNAL FEVER.—Patients suffering from this variety of malarial infection will present, as a rule, the following symptoms:

Prodromal.—The prodromal symptoms are: loss of appetite, slight headache, evanescent pains in the back and legs, nervousness, frequent urination, and a general feeling of malaise. As in the tertian and quartan infections, three stages may be distinguished.

The Cold Stage.—This generally commences with yawning, headache, slight nausea, perhaps accompanied by vomiting, and often intense nervousness. In the majority of cases there are no distinct chills, the patient complaining of creeping sensations along the spinal column, or slight flushes of cold, especially noticeable along the posterior portion of the buttocks and thighs. At the same time the headache increases, and the patient is generally profoundly depressed mentally. The skin presents the well-known appearance called "goose-flesh." The mucous membranes are cyanosed and the extremities cold. The legs and back ache, the pain as a rule being greatest in the lumbar region. The pulse is generally weak and increased in frequency, and is often irregular. The respirations are rapid and rather shallow. During this stage the temperature is elevated. As a rule, this portion of the attack does not last over half an hour, and the patient very seldom shakes with the chill, as in the tertian and quartan infections.

The Hot Stage.—Gradually the patient experiences a sense of heat, which comes first as localized flushings, but soon becomes general. The facial appearance is that common to fever, the eyes being suffused and brilliant, the face red, and the skin dry and

hot. Headache is intense, and there is present either great mental depression or nervous excitement. The pain in the back and limbs is often almost agonizing in character. The temperature is elevated and the curve characteristic. Nausea and vomiting are often present, the vomiting sometimes being very severe. Diarrhea sometimes occurs, and polyuria is frequent. The pulse is rapid, as a rule, full and dicrotic in character, the respirations hurried, and often appear to be difficult. This stage lasts for several hours, often for six or eight, and is succeeded by the stage of remission. During this stage the symptoms gradually decline in severity and finally disappear. The temperature returns to normal, generally going a degree or a degree and a half below normal, and slight sweating occurs. This, however, is not nearly so marked as in the tertian and quartan paroxysms. The headache often remains during the intermission.

As a rule, attacks of this fever occur toward evening, extend throughout the next day, and subside during the first hours of the third day, the paroxysm thus lasting 36 hours or more, and recurring every 48 hours.

The symptoms described are characteristic of this infection in only one particular, and that is the temperature curve. In uncomplicated cases the temperature curve is absolutely characteristic, and one not met with in any other disease, so far as known. At the onset of the fever the temperature rises suddenly to 103° or 104° F. Following the sudden rise there occur slight oscillations which cover several hours, during which time the temperature falls from one-half to one degree. This period of oscillation is followed by a distinct fall, or pseudo-crisis, the temperature dropping from 1° to 2° or even 3° . This fall is often considered by the physician as the true crisis. On the contrary, however, the fever again rises to a point higher than it had before attained, and then falls rapidly. This is the true crisis, in which the temperature falls, as a rule, below normal.

The temperature curve thus can be divided into five stages: (1) The initial rise, (2) the period of slight remissions, (3) the pseudo-crisis, (4) the precritical rise, and (5) the true crisis. This type of curve is well illustrated in Fig. 5.

Another point of marked difference between this type of fever and the tertian and quartan types is that the fever lasts for many

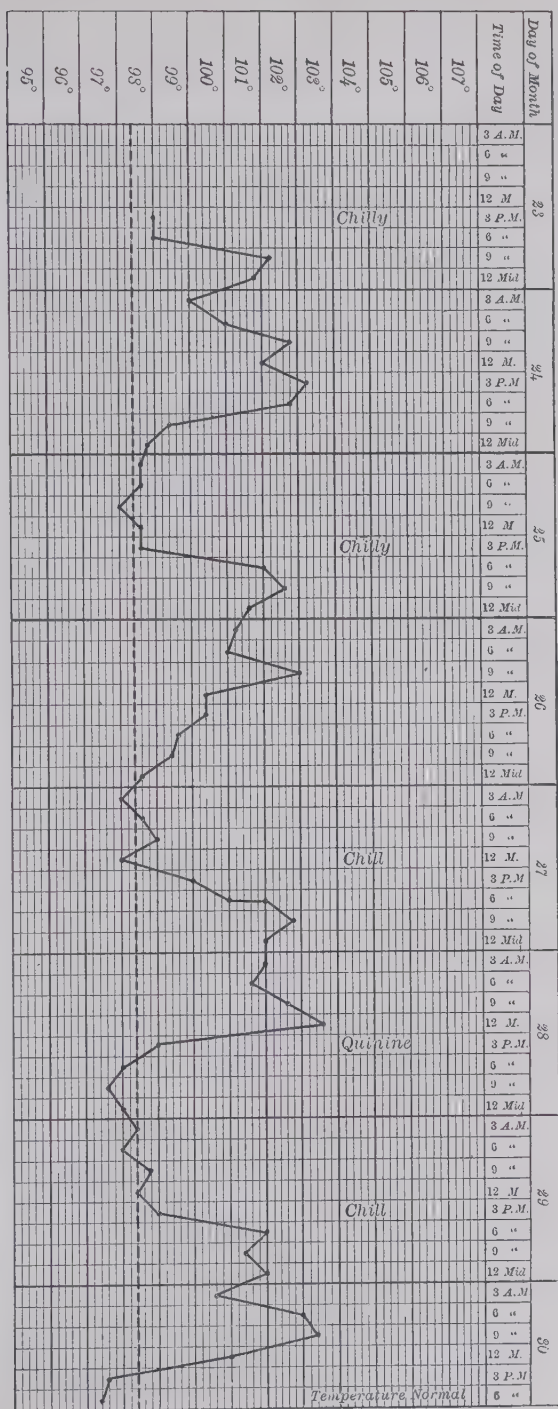


FIG. 5.—Temperature curve in tertian estivo-autumnal malarial fever. Note the peculiar curve and the length of the paroxysms. (From Estivo-autumnal Malarial Fever, by Craig.)

hours, generally over 24, and often from 38 to 40. That is, the paroxysm really covers two days.

In a large proportion of cases of tertian estivo-autumnal fever this characteristic temperature curve will be observed, but there are many deviations from it, due to several factors, among the most important being improper medication, double infections, or infections with more than one variety of malarial parasite, anticipation of the attacks or retardation, especially common in the pernicious forms, and slight elevations of temperature occurring between attacks.

A point to be emphasized is that the ordinary temperature charts, showing only the morning and evening temperature, are worse than useless as a guide in studying the estivo-autumnal fevers. The temperature should be taken at least every four hours, and better every three. A temperature chart taken morning and evening is very misleading, as will be seen by a study of the charts if simply the morning and evening temperature be noted.

THE QUOTIDIAN ESTIVO-AUTUMNAL INFECTION.—The quotidian infection differs but very little in its symptomatology from the tertian, except in the following particulars: As a rule, the quotidian cases are accompanied by more severe chilly sensations, and often there is a distinct chill; the sweating is also more pronounced, but is not so marked as in the simple tertian and quartan fevers. The temperature curve is entirely different. It consists essentially in an abrupt rise of temperature to 103° F. or more, succeeded by as abrupt a fall, the attack lasting, as a rule, only about eight hours. This temperature curve cannot be distinguished from that of a double tertian infection or a triple quartan. It is well illustrated in Fig. 6. The regularity of this curve does not long continue in most cases, as the attacks tend to run into one another, thus giving rise to a more or less continuous fever. This is especially noticeable in pernicious cases.

PERNICIOUS ESTIVO-AUTUMNAL MALARIA.—In this contribution it will be obviously impossible for me to describe minutely the large number of varieties of pernicious malaria which have been studied, and which have received their names because of the predominance of one or more symptoms. As stated, it should be distinctly understood that there is no parasite which produces only pernicious malarial fever, but that the same organism that produces the mildest

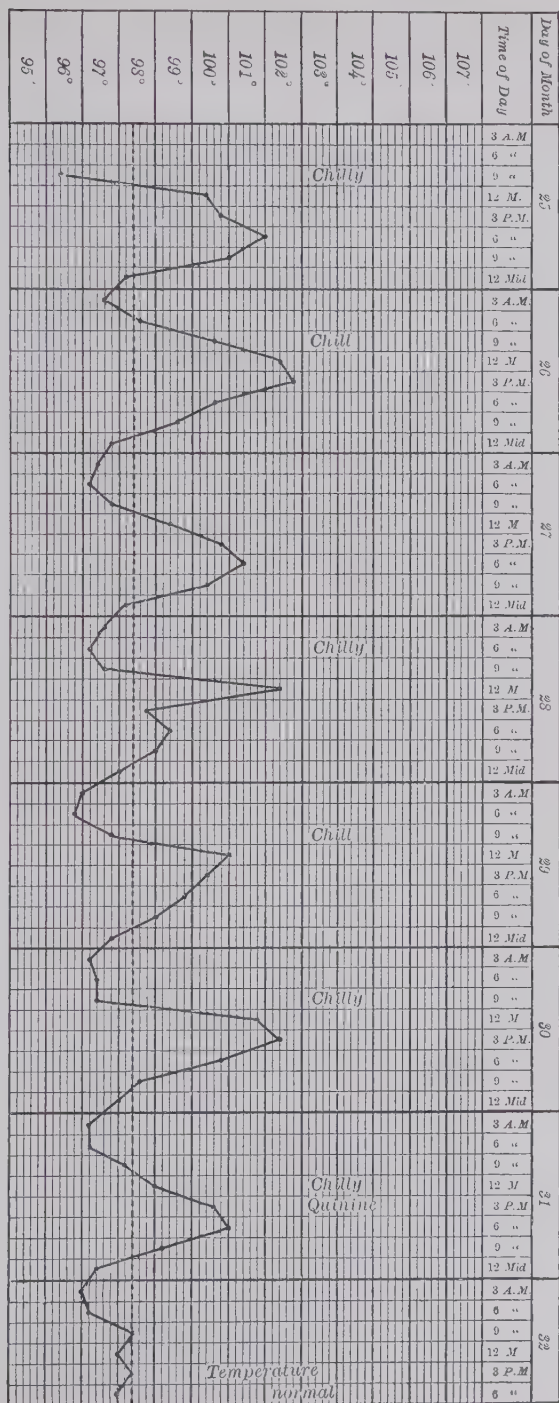


FIG. 6.—Temperature curve in quotidian estivo-autumnal malarial fever. (From Estivo-autumnal Malarial Fever, by Craig.)

case of malaria is capable of producing the most severe. As a matter of fact, however, the vast majority of pernicious malarial fevers are produced by the estivo-autumnal parasites.

The pernicious forms of estivo-autumnal fever are classified, as a rule, according to the most prominent symptoms which may be present. Thus we have the following forms: Comatose, hemiplegic, tetanic, delirious, ataxic, dysenteric, choleraic, algid, cardialgic, hemorrhagic, pneumonic, and bilious pernicious fevers. The most common forms, however, are the comatose and the algid.

The Comatose Form.—This form of pernicious malarial fever is generally due to the tertian or quotidian estivo-autumnal parasite, most frequently the tertian, and is characterized by the development of coma. In most cases the development of this condition is gradual, although it sometimes occurs suddenly. When it develops gradually, the patient has felt unwell for some time, and the attack begins with the same symptoms that are present in the ordinary malarial paroxysms. Nervousness, however, is, as a rule, more pronounced, and the patient is often greatly depressed mentally. A tendency to somnolence gradually develops, which deepens into stupor, and finally into coma. The unconsciousness is complete, the patient lying perfectly quiet, but there may be twitching of the limbs. The skin is generally yellowish in color and is hot and dry. The pupils are contracted equally, but they may be unequally contracted or equally dilated. The face is flushed and appears cyanotic. In old infections, however, the face may be pale. Slight spasmodic contractions of the muscles of the face are common. The respirations are slow and quiet, but they may be interrupted, rapid, or stertorous. The pulse is slow, full, and incompressible at first, but becomes rapid and weak as the condition advances. The sphincters are paralyzed, the urine and feces being passed involuntarily. In a few cases retention of urine may occur.

The duration of this condition varies from a few hours to three or four days. If untreated, a fatal result is almost always to be expected. Often, however, the patient will apparently improve for a short time; but this improvement is only apparent, the patient again sinking into coma.

The temperature in this form of pernicious malaria may be very variable. Some cases show a high temperature, which persists; others a comparatively low temperature; and in one case which I

observed, the temperature never went above 101° F. until a few moments before death, when it reached 103° .

The Algid Form.—The algid form of malaria is not uncommon in certain regions, and is characterized by a condition of collapse attended by profuse perspiration. At the same time the temperature is more or less elevated, but in some cases the temperature is subnormal. The appearance of the patient in this form of pernicious malaria is characteristic of collapse. The face is the typical "Hypocratic countenance," the cheeks and eyes sunken, the nose thin, and the skin pale and livid. The skin of the entire body is cold, cyanotic in appearance, and covered with a profuse perspiration. The lips and finger-nails are intensely cyanotic. The pulse is rapid, thready, easily compressible, and intermittent. The respirations are labored, irregular, and superficial, and become weaker and weaker as death approaches. Muscular weakness is extreme.

The mental condition of the patient is one of intense apathy to his surroundings, and the gravity of his condition is not, as a rule, appreciated by him. Death occurs generally in a few hours with all the symptoms of collapse.

The remaining varieties of pernicious infections it will be impossible to describe here, but, as has been said, they will present chiefly the symptoms which are embodied in their name; thus, in the dysenteric variety the chief symptoms are those of diarrhea, in the choleraic the chief symptoms are those of diarrhea accompanied by collapse, etc.

LATENT AND MASKED ESTIVO-AUTUMNAL FEVER.—Many patients suffering from estivo-autumnal fever present prominently such anomalous and atypical symptoms that the malarial condition is not recognized. Other cases present the infection in such a form that it is said to be latent, no symptoms of malarial fever being present, the infection being discovered accidentally during an examination of the blood. Both these conditions, however, are not common to the estivo-autumnal fevers, as tertian or quartan fevers can be latent in the system or masked by other disease processes. However, I believe that the latent and masked varieties are most commonly found in patients suffering from the estivo-autumnal infections, and have thus chosen to consider the entire subject under this heading.

There can be nothing more important in practising medicine in

malarious regions than to be able to recognize malarial disease at the earliest possible moment. Especially is this true where the estivo-autumnal parasites are endemic, as many of the conditions caused by these organisms are so insidious and dangerous to life.

There is only one absolutely sure way to recognize a latent malarial infection, or one masked by symptoms due to some other disease process, and that is by the microscopic examination of the blood. At this hospital (U. S. A. General Hospital, Presidio of San Francisco), the routine examination of the blood in every case is followed out, and during a period of three years 363 cases of malaria have been observed in which the parasites were present in the blood, but in which no diagnosis of the condition had been previously made. Most of these cases were masked by symptoms of some other disease, especially dysentery and gastro-enteritis. A considerable portion of them, however, occurred in patients who presented no evidence of malaria, and in which coexistent disease also presented no marked symptoms. In these latter cases, of course, the infection was latent.

Many of the patients, upon treatment with quinin, improved very markedly, the symptoms which were believed to be due to an existing dysentery clearing up, thus showing that the diarrhea was, in fact, due to the malarial parasites. In previous contributions I have given in detail the facts concerning these cases.¹

SUBCONTINUED OR REMITTENT INFECTIONS.—Certain cases, both of tertian and quotidian estivo-autumnal fever, instead of presenting the typical temperature curve which has been described, run a more or less continuous or slightly remittent fever. These cases have often been confused with typhoid fever, on account of the similarity of the temperature charts. (See Fig. 7.)

These subcontinued fevers may be due to a prolongation of the paroxysms so that they overlap each other, to a reduplication of the paroxysms, due to double infections or infections with various forms of parasites, or to an anticipation of the paroxysms, one beginning before the preceding one ends.

The symptoms in these cases are not different in kind from those occurring in the regular intermittent cases, but are generally more severe in character. The patient's appearance is often very

¹ Latent and Masked Malarial Fevers. Medical Record, February 15, 1902.

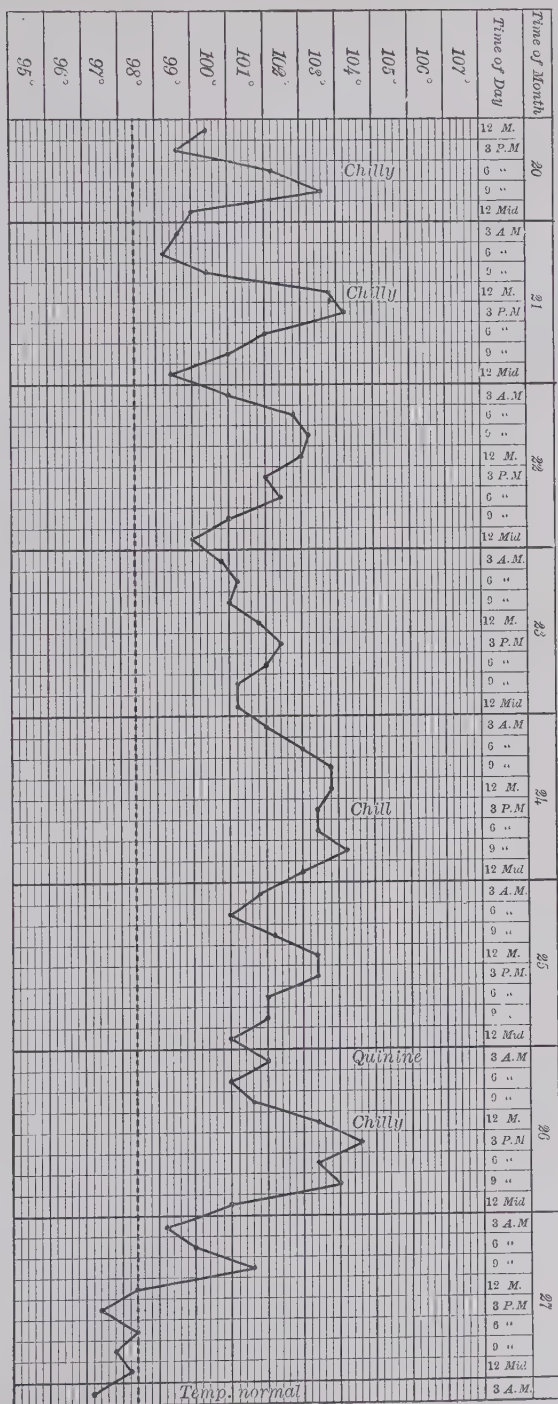


Fig. 7.—Temperature curve in estivo-autumnal subcontinued fever. The type of parasite present was the estivo-autumnal parasite. (From Estivo-autumnal Malarial Fever, by Craig.)

suggestive of typhoid fever, and I have seen cases that resembled this disease so much clinically that it would have been impossible for any one to have diagnosed between them. The resemblance is indeed startling, there being present epistaxis, gurgling and tenderness in the right iliac fossa, a roseolar eruption, an enlarged and tender spleen, besides the other symptoms which usually accompany typhoid fever. To this class of cases the name "typho-malarial" has been given by some observers. The temperature curve is very variable, slight intermissions corresponding to the end of the paroxysms being noticeable if the temperature chart be carefully studied. I have seen charts, however, of this condition which presented no marked intermissions, and which would have been taken at sight for the temperature curve of typhoid fever. If untreated, these cases may continue for several weeks, but generally a spontaneous cure or death occurs within three weeks.

DIAGNOSIS OF MALARIAL INFECTIONS

The diagnosis of the malarial fevers is a matter of the very greatest importance, especially in those regions where the estivo-autumnal infections are prevalent.

In the past the term "malaria" has covered a multitude of diagnostic sins, any puzzling case being apt to be called by this name. At the present time there can be no excuse for not making a diagnosis of malarial infection, no matter how puzzling the case may be, for, with the examination of the blood and the therapeutic test by quinin, we have all that is necessary absolutely to establish the diagnosis.

In arriving at a diagnosis of malarial infection we have two invaluable resources: (1) the examination of the fresh or stained blood, and (2) the therapeutic test by quinin. The most valuable of these two is the examination of the blood, which should never be neglected, especially when estivo-autumnal infections are suspected. In this class of cases the infection is apt to be so severe that we cannot wait the requisite time for the establishment of the diagnosis by quinin, while if the blood be at once examined, a quick diagnosis is assured. In the tertian and quartan cases the therapeutic test may be used with comparative safety to the patient, but even here the examination of the blood is preferable.

When possible, the blood should be examined fresh, and this

can be done in almost every case, as a specimen of blood will keep for several hours if wrapped in paper and carried in the vest-pocket, when it is necessary to transport it for a distance. If, however, stained specimens have to be used, the following method of securing smears is valuable: The ear or finger of the patient is carefully cleansed with alcohol, wiped dry, and pierced with a small lancet or knife. Several slips of the ordinary ribbed, white cigarette-paper are prepared, measuring about the width of the cover-glasses used. The edge of the paper is applied to the drop of blood upon the ear, being careful to have the ribs of the paper horizontal. The paper is then drawn lightly along the drop of blood and then along the cover-glass. It will be found that the paper adheres slightly to the cover-slip and can be drawn evenly across it, leaving a very thin, uniform blood smear. The cover-glasses are then dried and hardened in equal parts of absolute alcohol and ether, or in absolute alcohol alone, for 15 minutes.

Various staining methods have been devised, the most useful for clinical purposes being Jenner's stain, which can be purchased already prepared, or the simple stain of methylene blue and eosin, the cover-slips being immersed in the methylene blue for from 3 to 24 hours, and then stained for a few minutes with eosin. The malarial parasites will be stained blue, and the blood-corpuscles red.

There are many other methods of staining which are specially useful for showing the finer structures of the parasites; but as these are more or less complicated, they are not of as great service in routine work.

In examining the fresh specimens of blood the ear or finger is simply pricked, and the small drop of blood obtained is placed upon a glass slide and covered with a cover-slip. The sooner these specimens are examined the better, as the blood-corpuscles become crenated after being removed from the body, and often obscure the smaller forms of parasites. In examining such blood, special care should be taken not to mistake small hyaline spaces inside the corpuscles, which are due to retraction of the hemoglobin, for the malarial parasites. Crenations, if viewed from above, are often very hard to differentiate from minute hyaline organisms, but it will be observed in such cases that focusing up and down enlarges or makes smaller the suspected object, while the same does not occur in malarial organisms.

The therapeutic test by quinin can be absolutely relied upon, provided the drug is administered properly and the temperature chart carefully kept. This test, however, should never be used in the estivo-autumnal infections, for the danger of such infections becoming pernicious at any moment is so great that it is criminal to keep the patient in constant danger, simply to satisfy ourselves as to the effect of inadequate doses of quinin on the disease. In these cases the blood should always be examined at once, and quinin administered as promptly as possible. As Osler has well said, any fever which resists the action of quinin for a period of more than six days is certainly not malarial in character.

Diagnosis of Tertian and Quartan Cases.—Diagnosis, as a rule, in tertian or quartan malaria is not difficult. The regular occurrence of the paroxysms is generally sufficient alone to determine the character of the infection. There are cases, however, in which there are double infections, or infections with more than one variety of parasites, which may prove puzzling, but if the blood is examined there can be no excuse for not arriving promptly at a diagnosis.

Diagnosis of Estivo-autumnal Fevers, Quotidian Infection.—As a rule, the diagnosis of quotidian estivo-autumnal fever is not difficult, the regularly recurring chill and fever being very suspicious. However, in these cases we have to make a diagnosis between septic infections, tuberculosis, endocarditis, and several other conditions, and often this can only be done by an examination of the blood. In the same way a differential diagnosis between this form of estivo-autumnal fever and a double tertian infection cannot be made without such examination.

Tertian Infections.—Diagnosis of these infections is often impossible clinically. Provided we have a typical infection showing the characteristic temperature curve, a diagnosis could be very easily made, as in no other disease is such a temperature curve seen. However, a vast number of these cases show irregularities in the temperature curve, absence of chills and the other characteristic signs of malarial infection, and a diagnosis without an examination of the blood will often be found impossible. In no class of cases is the examination of the blood so valuable as in the tertian and pernicious forms of estivo-autumnal malarial fever.

Pernicious Infections.—Pernicious infections so often resemble other forms of disease and are so dangerous to life that a diagnosis

should be very quickly arrived at. It is an undoubted fact that many lives have been sacrificed because the attending physician was unable to diagnose pernicious malarial fever. I have met with several cases in which the infection was not discovered until just before death, too late for any remedial measures to be taken.

It may be urged that not every physician is capable of recognizing under the microscope the various forms of malarial parasites; and this is unfortunately true. But at the same time, in many places where such deaths have occurred, an examination of the blood could have been made by a specialist, and the death of the patient averted. It is certainly criminal for a physician to lose a case of pernicious malarial fever when he has neglected to do his utmost in the way of a blood examination. As I have said, these cases are often so misleading in their symptomatology that it is impossible clinically, until too late, to arrive at a clear solution of the condition present. A few moments' study of the blood will often demonstrate the nature of a case which has been puzzling the attending physician for days.

In the pernicious cases the therapeutic test by quinin will obviously be impossible, as the length of time required will endanger the life of the patient.

DIFFERENTIAL DIAGNOSIS OF MALARIAL INFECTIONS

The differential diagnosis of the malarial fevers, especially the estivo-autumnal types, from other disease processes, is a most important subject. Owing to the limited space I cannot discuss fully all of the various conditions which have to be differentiated from malarial infections, and therefore will only touch upon the most important.

Typhoid Fever.—Perhaps there is no one disease which has been so often mistaken for malarial fever, especially estivo-autumnal fever, as has typhoid. Our late experience in the war with Spain has abundantly proven that this is so. At least three-quarters of the fevers occurring in the Southern camps during 1898, and diagnosed "remittent malarial fever," were in reality typhoid, as shown by the blood examination and the Widal test. Many malarial infections show symptoms which no doubt are very hard to distinguish from those occurring in typhoid fever, and clinically the diagnosis between the two is often so difficult that there is much

excuse for a mistake; at the same time, now that we have the Widal test, such a mistake should never be made. In malarial cases which simulate typhoid, or *vice versa*, an examination of the blood and Widal test will at once clear up the diagnosis. To be sure there are cases of typhoid which do not react to the Widal test, but these are so very rare as to be of almost no diagnostic importance. When neither the Widal test nor a microscopic examination of the blood can be made, the therapeutic test by quinin should be utilized. Any fever which resists the action of quinin for a period of over seven days cannot be of malarial origin, providing the quinin be properly administered.

Combined Infections.—Lyons has collected all the recorded cases of combined typhoid and malarial fevers which have been shown to be such by the Widal test and the examination of the blood. From his report it is proven that all varieties of malarial fever may complicate typhoid, the tertian and the estivo-autumnal being the most common. The only case of combined quartan malarial fever and typhoid that I know of was observed by myself at Chickamauga Park, and reported upon.¹ Cases of combined infection are very rare, and should only be considered as such when the blood is positive for the Widal reaction and at the same time malarial parasites are present.

Tuberculosis.—Many cases of malarial infection simulate tuberculosis in that the temperature charts are similar and the patient is emaciated and has a more or less chronic cough. The examination of the sputum for the tubercle bacillus and of the blood for the malarial parasites would at once clear up the diagnosis in such cases.

Dysentery.—It would seem at first sight that it would be impossible to mistake a case of dysentery for malarial fever, but the result of my own observations and of those of others leaves no doubt in my mind that there is a malarial dysentery, due to the special localization of the parasites in the glands of the mucous membrane of the intestine. I have observed many such cases in soldiers returning from the Philippine Islands. The examination of the blood will at once decide the presence of malarial infection, and treatment with quinin will, in these cases, cure the dysenteric symptoms.

¹ Philadelphia Medical Journal, June 17, 1899.

Yellow Fever.—In regions in which yellow fever is prevalent some cases of pernicious malarial fever very closely resemble such infections. The yellow tint of the skin, the severe vomiting, the high temperature, and very often the occurrence of albumin in the urine, lead to a suspicion of the presence of yellow fever. In these cases the examination of the blood is very important, and the diagnosis of yellow fever is always open to doubt unless such examination has been made.

Among the other diseases with which the malarial fevers may be confused may be mentioned hepatic abscess, ulcerative endocarditis, pneumonia, Weil's disease, and suppurative processes in various portions of the body. These may all be differentiated by the microscopic examination of the blood.

The pernicious malarial fevers often simulate very closely cerebral apoplexy, and this is especially true of the comatose form. The main points to be relied upon in making the diagnosis are the high fever, the age of the patient, and the splenic enlargement. A microscopic examination of the blood should be made at once in these cases.

In the tropics sunstroke may be confused with pernicious malarial attacks, but the examination of the blood will at once clear up the diagnosis.

TREATMENT OF MALARIAL INFECTIONS

The treatment of malarial fever consists in the prophylactic and the remedial treatment.

PROPHYLAXIS.—As we now know that the mosquito transmits malarial infections, and that, in all probability, such infections cannot exist without the presence of this insect, it is at once obvious how important have become the measures used for its extermination.

The time at which the mosquito is most susceptible to destruction is during the larval stage. The most useful measures are the following: Draining of their breeding-places, treatment of mosquito pools with kerosene, and the introduction of small fish into the breeding-places. Where it is possible, the filling up of stagnant pools of water, or a complete drainage, is most efficacious. Where such measures cannot be taken, the spraying of kerosene upon the surface of the water, thus shutting off the supply of oxygen from the larvæ, should be systematically pursued. Howard has deter-

mined that the quantity of kerosene needed is approximately one ounce to every 15 square feet of water surface, and the application need not be renewed more than once a month. The introduction of fish in places where kerosene cannot be used, as in drinking-water, has proven valuable in many places. Almost any small fish will answer, but the most valuable are carp and the common "stickle-back."

In malarious districts the organization of mosquito brigades, as recommended by Ross, should be undertaken, and a systematic and careful effort made to obliterate all breeding-places of the insect.

PERSONAL PROPHYLAXIS.—Persons living in malarious districts can, by careful attention to several small details, render themselves very much less liable to infection. Thus, the windows and doors of houses should be thoroughly screened; patients suffering from malaria should be isolated in a screened room, so that the infection can travel no further; the beds should be protected by mosquito netting; as far as possible travelling should not be done at night; and as protection for the hands and face during the day, where mosquito net cannot be used, the smearing upon the skin of certain oils, such as oil of pennyroyal or eucalyptus, will be found useful. If, as in the tropics, the residence be near native quarters, great care should be taken in destroying the breeding-places of mosquitoes, which are very numerous around such habitations.

REMEDIAL TREATMENT.—The remedial treatment of the malarial infections may be summed up in the one word "quinin." While many other drugs have been recommended, none has as yet been discovered which can approach it in efficacy.

Tertian and Quartan Infections.—In tertian and quartan infections my preference is to give a single large dose of the drug (25 to 30 grains; 1.5 to 2 grams) at the commencement of the sweating stage. It is not well to give the drug at the commencement of the chill, as it will aggravate the headache and nervous symptoms. Given at the commencement of the sweating stage, it attacks the parasites during their period of least resistance,—that is, the young segmenting bodies,—and will nearly invariably prevent the next paroxysm. After the initial large dose, 10 grains (0.65 gram) of quinin should be given every day for at least a week, and 5 grains (0.3 gram) every day for two or three weeks following. Such

treatment will invariably cure these infections; and it is not necessary for the patient to remain in bed, although it is preferable for him to do so for the first day or so. As a rule, in quartan infections treatment has to be continued for a longer period than in the tertian.

Estivo-autumnal Infections.—As in these infections the time of the paroxysm cannot be so accurately determined, it is better practice to give the quinin in divided doses. My method has been to give 5 grains (0.3 gram) of the drug every four hours for at least a week. As soon as the active symptoms have subsided this dose may be gradually diminished, but the treatment should be continued for several weeks. It should be remembered that these infections are often very resistant to treatment.

At the commencement of the attack the bowels should be opened with calomel, and the patient kept in bed until active symptoms have subsided. Pernicious symptoms should be carefully looked for and quinin used hypodermically if necessary. One of the most common mistakes in the management of this type of infection is the too early abandonment of treatment.

The form of quinin used should be either the sulphate or the hydrochlorate, preferably in solution. If the solution cannot be used, capsules are much better than pills.

Pernicious Malaria.—In pernicious cases of malarial infection it is necessary to give quinin as promptly as possible, and in such cases the use of the hypodermic syringe is indicated. The solution generally used is the following: Hydrochlorate of quinin 5 grams (75 grains), distilled water 10 c.c. (2.5 drams). In this solution 1 c.c. (15 minims) contains 0.5 gram (7.5 grains) of quinin. Great care should be used in making the injection, as serious abscess formation has followed the hypodermic use of this drug. The syringe should be thoroughly sterilized and also the area of skin selected. The gluteal region should be selected, the injection being made deep into the muscles. Despite all precautions the hypodermic injection of quinin is always followed by much pain and discomfort, and more or less induration around the site of injection is to be expected. The intravenous injection of quinin has been recommended, but is seldom used.

Among the substitutes for quinin may be mentioned euchinin, a tasteless preparation which is just as efficacious, but is objectionable on account of its great cost. The only advantage it has is the

absence of the bitter taste. Methylene blue has been much vaunted in the treatment of malaria. I have seen it effect some cures, but it is much less valuable than quinin. The dose is from 8 to 16 grains (0.50 to 1 gram) in 24 hours. Phenocoll, a derivative of phenacetin, has proven useful in the milder forms of tertian and quartan malaria, but it is of no use in the severer infections.

Conclusion.—In conclusion I wish to again emphasize two points: (1) The infinite importance of the examination of the blood in all malarial infections and in other diseases occurring in patients who have lived in a malarious locality; and (2) the danger which is always present in estivo-autumnal infections of the development of pernicious and rapidly fatal symptoms.

CLINICAL TYPES OF PNEUMONIA, WITH SPECIAL REFERENCE TO ABERRANT FORMS

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I HAVE no desire in this paper to give an exhaustive account of pneumonia. I wish rather to dwell upon some of the peculiarities and difficulties which are most frequently encountered in dealing with this important disease. As far as possible I shall speak of the types of the affection which have come under my own immediate observation, with reference to illustrative cases.

Lobar pneumonia is now universally recognized as one of the acute infective diseases, the different lesions and clinical symptoms being the direct result of the action of a specific virus. I do not wish to enter minutely into the bacteriology of the subject, but I would emphasize the fact that the pneumococcus discovered in the saliva by Sternberg in 1880 and rediscovered by Fraenkel in 1884, is undoubtedly the causal agent in almost all cases of pneumonia. In typical cases of lobar pneumonia it is practically the only organism present; it is doubtful, indeed, if the pneumococcus is ever absent from true lobar pneumonia, though it may be associated with other pathogenic bacteria. It is important to note also that the pneumococcus may cause bronchopneumonia as well as lobar pneumonia, especially in children. In this connection it is particularly interesting to note that the late Dr. Washbourn in his posthumous Croonian Lectures, recently delivered at the Royal College of Physicians, found that the culture strains derived from lobar pneumonia tended on inoculation in rabbits to produce *fibrinous* inflammation, while those derived from bronchopneumonia, on the other hand, produced *cellular* inflammatory products. Many bronchopneumonic and mixed forms are probably due to association of the pneumococcus with other organisms, particularly those of influenza, septicemia, diphtheria, and plague, and probably also enteric fever.

In considering the different clinical types of this disease, it is important to note that there is a marked difference in the vitality of individual pneumococci, the majority dying, even in the most suitable culture medium, if the temperature is reduced much below that of the body, while others remain active even at 20° C. It is also important to observe that it is these resistant types that are the least virulent.

In considering the symptoms of pneumonia, one must note that the pneumococcus produces practically no detectable soluble toxin, and so differs markedly in this respect from the bacillus of diphtheria and from that of tetanus. Of course, it is possible that a toxin may be produced, but it is so unstable that it is readily destroyed and cannot therefore be isolated. Virulent forms of pneumococci can readily be converted by cultivation into absolutely avirulent types, and can be reconverted into virulent forms by passage through susceptible animals.

Light has been thrown upon the causation of pneumonia by the interesting discovery of Sternberg, who demonstrated the presence of virulent pneumococci in the saliva of healthy individuals, which, when injected into a rabbit, produced fatal septicemia; he found them in 20 per cent. of healthy people, while the late Dr. Washbourn recently found them in as many as 30 per cent. The pneumococcus may also frequently be found in the lungs of healthy people. The existence of the virus in the mouths of healthy persons, and still more its existence in their lungs, seems obviously to have a very important bearing on the origin of the disease: a chill may simply lower the resisting power of the lung to the pneumococcic invasion; and, as there is little or no defence against this invasion, once the germs have reached the alveoli, one can readily understand why pneumonia should be one of the most wide-spread and common of acute diseases. In the future it may even be found advisable to recommend the general and routine use of antiseptic mouth-washes and gargles as a prophylactic measure in the case of persons exposed to cold, depressing influences, impure air, and other predisposing conditions.

As regards the metastatic effects of the pneumococcus, it is important to remember that the germs may pass through the lungs and set up inflammation in some distant part, without leaving a trace of inflammation in the lung itself. Thus by passing a catheter

through the larynx into the trachea, and thereby introducing a virulent culture of the pneumococcus, one may produce pleurisy and pericarditis and other lesions in an animal, while the lungs themselves may be found perfectly normal. This has been done by Dr. Washbourn and other observers. The significance of this fact in connection with pneumococcic empyemas in children is obvious. The more one studies recent researches, the more one is convinced of the virulent qualities of this deadly bacillus, which by no means limits its operations to the lungs, but is also a potent cause of pleurisy and empyema, pericarditis, endocarditis, meningitis, and otitis media. The acute middle-ear disease following influenza may possibly have the same origin. It is indeed difficult to exaggerate the multiplicity of the lesions that may be ascribed to its action. May not also the various types of pneumonia, to be hereafter described, be due mainly to the varying degrees of virulence possessed by the invading pneumococcus?

Some diseases are particularly prone to be followed by pneumonia: I might particularly mention influenza and typhoid fever. As showing the effect of influenza, it is a remarkable fact that the death-rate from pneumonia in males, as shown by the British Registrar-General's returns, rose with a bound from 1206 per million in 1889, to 1731 in 1890, and to 1798 in 1891 (coincidentally with the first two general epidemics of influenza), while among females the mortality rose from 848 per million in 1889 to 1165 in 1891. In the case of typhoid fever the pneumonia usually occurs in the third or fourth week. It is probable that both influenza and typhoid fever exercise a special action in lowering the resisting power of the lung-tissue to the invasion of the pneumococcus. This is borne out by the fact that although pneumonia may attack the strongest persons, yet any condition of depressed vitality, due to fatigue, injury, starvation, alcoholism, etc., renders the person much more liable to the disease. This no doubt explains the frequent history of exposure to cold, which probably acts by lowering the resisting power of the lung and thus affords a suitable opportunity for the potent and ubiquitous pneumococcus.

The fact that the right lung is so much more often attacked than the left—the proportion being about seven to three—is probably due to the fact that the right bronchus is larger and less oblique than the left, and more directly continuous with the trachea,

As regards the clinical features of pneumonia, I shall not describe the well-known characteristic symptoms, but shall confine myself to mentioning a few points that I have found of value in the diagnosis of doubtful cases, and shall then go on to deal with some of the aberrant types that one occasionally meets with in both hospital and private practice. Though in the large majority of cases the onset of the disease is sudden, with the well-known rigor and abrupt elevation of temperature, yet in a small minority the disease is preceded by premonitory symptoms which may last for one or two days, or even longer. These early symptoms are headache, malaise, loss of appetite, aching of the limbs,—such as frequently usher in other infectious diseases. These cases of insidious onset are fortunately exceptional, but their existence must not be overlooked: they are more frequently met with in private than in hospital practice, and are familiar to medical men engaged in general practice. One does not usually see these cases in the hospital until the disease is fairly well advanced, though we occasionally get a history which suggests a gradual onset not unlike that of enteric fever.

When the patient has been ailing more than a day or two, the disease is commonly and often rightly regarded as influenzal in origin, and certainly these insidious cases have been much more commonly observed since the introduction of epidemic influenza into this country some ten or twelve years ago. The French term “*la grippe*” is by no means applicable to all cases of influenza met with during the last few years, many of which arise insidiously and without the sudden elevation of the temperature to 104° or 105° F., which was such a marked characteristic of the first two epidemics.

It is usually stated that a convulsion replaces the initial rigor in the case of children. I took the trouble to analyze the cases of pneumonia admitted into the children's ward at King's College Hospital, and found that the initial symptom in children was much more commonly vomiting than convulsion. One of the most important diagnostic symptoms of an obscure pneumonia is the pulse-respiration ratio, which is commonly three to one, instead of four to one.

Leukocytosis is another valuable diagnostic symptom, the leukocytes usually numbering from 12,000 to 40,000, instead of the normal 9000, per c.mm. This leukocytosis readily distinguishes pneumonia from typhoid fever and influenza. Stengel showed that

the increase was chiefly in the polymorphonuclear cells, which have the most potent phagocytic action. It may here be mentioned that the absence of leukocytosis is generally regarded as a most unfavorable sign, the increase of leukocytes indicating the natural healthy reaction of the organism to repel the invader.

Cough and expectoration may be absent altogether in pneumonia, even in adults, and it is generally regarded as an unfavorable symptom, as it leaves more inflammatory products to be absorbed by the pulmonary capillaries. In children under 8 years of age there is of course no expectoration, and we are thus deprived of the rusty sputum which is such an important diagnostic symptom. It is generally true that the more intense the initial rigor, the more virulent the poison and the more severe the disease. On the other hand, Dr. Kingston Fowler states that there is no definitive relationship between the number of pneumococci and the degree of pyrexia or the severity of the disease,—which apparently depend more upon the degree of virulence than upon the actual number of the diplococci.

Distinct hemoptysis occurs in a few cases, the patient bringing up bright arterial blood: this probably denotes intense congestion of the pulmonary tissue, and is not in itself an unfavorable symptom, nor should it necessarily cause a suspicion of tuberculosis.

I shall allude to the question of temperature when I speak of the more atypical forms of the disease.

The presence of herpes round the lips is one of the most interesting symptoms, principally on account of its great but inexplicable importance in regard to prognosis,—the mortality being only 7 per cent. in herpetic as against 25 per cent. in non-herpetic cases.

The physical signs of pneumonia are too well known and characteristic to be described. I should like, however, to mention the necessity of always examining the apex as well as the base of the lung, particularly the posterior apex, whenever the symptoms are suggestive of acute lung inflammation. I happen to know of more than one case in which the condition was overlooked owing to the bases alone having been examined. In my experience apical pneumonia is not so uncommon as is generally supposed, particularly in children. One observer suggests the following probable explanation why such cases are overlooked: the front of the chest is examined as a matter of course; the patient is then asked to sit up,

the night-dress is rolled up toward the neck, generally to the level of the spines of the scapulæ, and the lungs below this level are examined; the supraspinous fossæ, being above the fold of the night-dress, are thus sometimes missed. It should be a matter of routine in every chest case to pull down the night-dress over the shoulders and examine the posterior apices. This procedure applies particularly to private practice, as in hospitals the patient is usually stripped to the waist.

It is also worth noting that several days may elapse before any physical signs manifest themselves, owing to the inflammation commencing in the central portions of the lung and advancing slowly toward the surface. I recently saw a very severe case in a young girl with all the typical symptoms of the disease, but in whom the characteristic signs did not appear until the fifth day.

In a small proportion of cases—the so-called *central* pneumonias—the disease never reaches the surface at all, undergoing the processes of congestion, red hepatization, gray hepatization, and resolution, in the interior portions of the lung. These cases, though presenting all the typical symptoms of pneumonia, show none of the physical signs. I recently saw such a case at King's College Hospital in a woman aged 62: there was no dulness and no auscultatory signs; the symptoms, however, were quite characteristic, there being high and continuous pyrexia and the temperature coming down by a sharp crisis on the seventh day. The patient made a good recovery.

I lately saw a man, aged 42, in whom on the sixth day of the disease a little friction developed in the right axilla, with slight impairment of the percussion note, but with no tubular breathing. This was probably a case of "central" pneumonia in which the inflammatory process had come to the surface toward the end of the disease.

It is generally believed in England, and my experience inclines me to support this belief, that apical pneumonia is more fatal than the common basal type. I have seen a considerable number of apical cases: delirium has been frequently a prominent symptom, while there has been a general tendency to an asthenic and toxemic condition. Apical pneumonias in children, on the other hand, seem to do well. A number of my apical cases have been in alcoholic subjects, and most of these have succumbed. It is said that apical pneumonia less readily undergoes resolution.

As regards physical signs, it may be mentioned that in the pneumonias of children crepitation may be absent throughout. It is also worth noting that auscultatory signs are occasionally present over the sound lung—from conduction, and may thus lead to a wrong diagnosis of double pneumonia. The typical tubular breathing may never be heard at all, particularly in influenzal pneumonias. This was the case, I believe, with the late Duke of Clarence. I shall refer to this point again in speaking of *massive* pneumonia. In the early stage of pneumonia, before consolidation has actually taken place, the breath sounds may be much feebler than over the healthy lung, but they are even then generally harsh and of a broncho-vesicular type on asking the patient to breathe deeply. In these cases, in which the physical signs are indefinite, intensification of the heart-sounds over the area of consolidated lung is a physical sign of some importance.

Before leaving the question of physical examination in cases of pneumonia, I should like to emphasize the importance of the danger of over-examination. I have known of patients succumbing immediately after examination. I believe it to be extremely dangerous in the later stages of the disease to ask the patient to sit up for the purpose of examining the pulmonary bases. Owing to the lower lobe coming well forward in the lower axillary region, it is generally possible to satisfy one's self of the site of the disease by simply turning the patient slightly on to the sound side: any serious involvement of the upper or middle lobe will soon manifest itself in front. In any case, it is infinitely more important to conserve the patient's strength and avoid the possible risk of cardiac failure than to satisfy one's self as to the precise extent of the inflammatory process, especially as no means, with which we are acquainted, can in the least degree check the spread of the disease.

Coming now to aberrant forms, I should like, in the first place, to refer to *abortive* or *larval* pneumonia. In a small number of cases the patient has the initial symptoms of pneumonia, some pyrexia, herpes, and some indefinite physical signs lasting for a day or two. The temperature then suddenly falls, the patient perspires, and convalescence takes place: the disease seems to have aborted. Such cases are apt to occur at a time when there appears to be a pneumonia epidemic. Influenzal pneumonias sometimes only last from three to five days. I recently saw a young porter, aged 22. The

day before admission he had a slight rigor; two hours later he felt a sharp cutting pain in the chest; next morning the temperature rose to 102° F., and there were a few fine crepitations in the lower part of the right axilla and below the angle of the right scapula. That evening there was present at the left base increased vocal fremitus, some dulness, bronchial breathing, bronchophony, and fine crepitant râles. The next day (the third of the disease) the attack appeared to abort, the temperature fell to normal, the physical signs rapidly cleared up, and on the fourth day the patient felt bright and cheerful and practically well. He was able to leave the hospital three days later.

It is quite possible that a certain proportion of those cases so frequently described under the vague term "congestion of the lungs" belong to this category, though the term is probably also applied to cases of capillary bronchitis.

Some authors refer to a type which they term *latent* pneumonia. There is no doubt that in some cases of old people, persons weakened by starvation, alcoholism, or debilitating illnesses, particularly chronic Bright's disease, the onset may be very insidious and the symptoms so slight that the case may not be recognized until the post-mortem examination.

Medical officers in lunatic asylums have told me that in dementia and other forms of chronic insanity a pneumonia may run its full course with a subnormal temperature. I recently performed a post-mortem examination in the case of a man who had died of pyloric carcinoma, and found the lower lobe of one of the lungs completely consolidated, though such a condition had not been suspected during life.

We now come to a type which has given rise to much discussion, and which has been described by Dr. Dreschfeld and others as *migratory* pneumonia. This is characterized by the successive invasion of different portions of the lung, while the physical signs disappear from the parts first attacked; the affected portions clear up with great rapidity, while other portions in turn become affected with congestion or consolidation, the extension to one part coinciding with resolution in another. The course of such a case, it is said, may be prolonged for several weeks. Sir Douglas Powell states that this migratory pneumonia probably coincides with the pythogenic pneumonia described by the late Dr. Murchison, which is charac-

terized by a more insidious onset, a more fluctuating type of temperature, an incomplete crisis, the physical signs of imperfect consolidation, the asthenic condition of the patient, and its peculiarity in attacking successively different portions of the lung. In fatal cases—and such cases are frequently fatal—Dr. Dreschfeld found the affected portions of the lung teeming with capsulated diplococci. Personally, I am of opinion that these cases may ultimately be proved to be simply forms of septic bronchopneumonia. Last year I was called to see in consultation a well-developed, athletic man of 22 years. He was said to have had influenza some weeks before coming under observation; there was a high, remittent pyrexia, the evening temperature rising to 104° and even 105° F.; there was marked dyspnea, an anxious expression of face, and a rapid, feeble pulse. There was some cough and expectoration; the sputum contained both pneumococci and streptococci, while the blood obtained from the lung by an exploring syringe also contained pneumococci; the blood taken from the lobe of the ear was found sterile. There was a moderate degree of leukocytosis. There were areas of dulness and bronchial breathing in the right upper lobe, left lower lobe, and smaller patches elsewhere. Some of those patches cleared up, to be replaced by other dull areas elsewhere. The temperature continued to be of a high remittent type until the twelfth day, when he succumbed from cardiac failure.

The question of *relapse* in pneumonia has also been provocative of much debate and difference of opinion. Professor Osler, of Baltimore, asserts that relapse in cases of pneumonia is most uncommon, and that its occurrence must even be regarded as doubtful: he thinks the secondary fever ought to be regarded as due, not to true relapse, but to delayed resolution. Dr. Kingston Fowler, on the other hand, is of opinion that relapse may occur, with fresh invasion of the lung-tissue. I shall here quote three cases in support of the theory of relapse, two of which have recently come under my own observation, the third being under the care of my friend Dr. Arthur Davies at the London Metropolitan Hospital. The first was that of a woman, aged 30 years, who was admitted to King's College Hospital, in May, 1902. She had a rigor and backache one week before coming under observation. On admission there were signs of consolidation of the left lower lobe, and also scattered bronchitic signs throughout both lungs. After a week's pyrexia there were ten days

of normal temperature, during which the lung signs cleared up. There was again a period of pyrexia, lasting seven days, during which the dulness reappeared at the left base. The possibility of pleurisy with effusion was negatived by exploration. The second case was that of a girl, aged 13 years, who was under my care at the Royal Chest Hospital with signs of consolidation of the left lower lobe, and of acute pericarditis. The physical signs at the left base disappeared, the pericardial friction-murmur persisted, but the general condition of the patient had much improved and the pyrexia had subsided. She appeared to be rapidly recovering and was believed to be out of danger. A few days later she again became worse, the physical signs of consolidation developed at the right apex, and she died on the following day. At the post-mortem examination it was found that the left lung was almost healthy, but that the upper lobe of the right lung was completely consolidated; there were the usual post-mortem appearances of acute pericarditis, and there were also recent vegetations on the aortic valve. Sections of the inflamed lung and pericardium contained pneumococci. In the third case there were signs of consolidation of the left lung, beginning at the apex and gradually spreading to the base; these signs entirely cleared up and the inflammation seemed to have completely resolved; the patient was doing well, but again became worse, and signs of consolidation reappeared at the left apex, while meningitic symptoms also developed. The patient died, and at the post-mortem examination there was found consolidation of the left upper lobe and also acute meningitis. From the semipurulent exudate covering the meninges cultures of pneumococci were obtained.

These considerations naturally lead us to the question of *delayed resolution*. It is generally recognized that the resolution, which as a rule immediately follows the crisis, may be postponed to the fourth, fifth, or even tenth week. It is difficult to give an explanation of this delay in the absorption of inflammatory products. It is said that the coexistence of old-standing valvular heart-disease as a complication tends to the long-continuance of the stage of red hepatization as well as that of resolution. A case in point came under my observation last year: it was that of a woman aged 31 years who was admitted into King's College Hospital with all the signs of consolidation of the left lower lobe. The illness had a definite onset one week before admission. Twelve months

previously she had been an in-patient with aortic incompetence. There was a typical history of sharp pain in the right side commencing one week before admission and followed a few days later by cough, shortness of breath, and rusty blood-stained sputum. The patient had a typical pneumonic aspect with marked dyspnea (44 respirations per minute). There were all the signs of consolidation of the left lower lobe with a loud friction rub. A few days after admission there were dulness and tubular breathing at the right base. There was high continuous pyrexia for four weeks and milder pyrexia for three weeks longer. There was dulness with tubular breathing and crepitant râles at both bases for eleven weeks and more or less acute dyspnea throughout. The lungs then gradually cleared up, the dyspnea completely subsided, and the patient made an excellent recovery.

I must just refer briefly to the clinical type known as *alcoholic pneumonia*. It deserves special mention mainly on account of its significance in regard to prognosis. The mortality in cases of pneumonia occurring in true alcoholics is as high as 70 per cent., in contradistinction to the average mortality, which is about 20 per cent.

Restlessness, delirium, tremor, and insomnia are often marked features, and such symptoms should put the physician on his guard and induce him to make very careful inquiries regarding the previous habits of the patient. If a strong alcoholic history is obtained, the physician may have to devote himself almost solely to his patient until the crisis is past.

There is little to be said regarding the so-called *inhalation pneumonia*, which is one of the grave dangers in operations connected with the upper portion of the respiratory tract, and which is a frequent mode of fatal termination in cases of laryngeal paralysis. This form is generally of the bronchopneumonic type, as one would expect from the fact that the exciting cause, such as a particle of food or other septic material, is apt to lodge at the termination of individual bronchioles and so set up inflammation of the corresponding lobules. Such a pneumonia may terminate in abscess-formation. A case of the latter is published in last year's King's College Hospital Reports (1902), in which numerous other septic organisms, in addition to the pneumococcus, were found in the walls of the abscess-cavity.

I shall now refer to the interesting clinical type known as *massive* pneumonia. This is a rare but well-marked form, in which the bronchi as well as the alveolar spaces are filled with fibrinous exudate. This type has attracted much attention on account of its liability to be mistaken for pleuritic effusion, the physical signs being somewhat similar, particularly the auscultatory signs, which are negative in both. I have seen only one case, which was readily diagnosed by the symptoms and appearance of the patient which were quite characteristic. These cases are said to be often very severe, and frequently fatal; there may be no cough or expectoration.

Since the introduction of Russian influenza, some ten years ago, certain types of pneumonia have become so common that a special type called *influenzal* pneumonia has been described. I have already alluded to the occasional occurrence of aborted pneumonias after influenza. Influenzal pneumonias are very apt to be atypical; they may, for instance, be accompanied by a profuse mucopurulent expectoration with almost no rusty sputum while the temperature is apt to be remittent and irregular in type. Professor Leyden describes influenzal pneumonias as often running a peculiar course, stating that the severe pain in the side, and even the dyspnea, may be absent, while the typical sputum is often wanting and the local process often atypical, being of a migratory and catarrhal type, with a lobular distribution in many cases. Tubular breathing is often absent. The German authorities lay stress on the prominent part played in these cases by the *Streptococcus pyogenes*, while the discovery by Pfeiffer in 1892 of the *Bacillus influenzae* in the purulent bronchial secretions must be regarded as strong evidence of the existence of a specific primary infection by this bacillus, either alone or in association with the pneumococcus. It is noteworthy that pneumonia has become much less common during the last few years than in the early epidemics of influenza. Either the virulence of the bacillus has become less, or more probably we have, by the repeated attacks of influenza, become partially immune to the graver manifestations.

We now come to the great question of *complicated* pneumonias. Any complication in pneumonia is of grave import. Huss states that the mortality of complicated cases is nearly four times greater than that of the uncomplicated cases. A certain degree of *bronchitis* is constantly present in pneumonia, but severe bronchitis must al-

ways be regarded as a serious complication, owing to the increased air obstruction and also to the increased strain upon the right heart. Last year I analyzed 45 successive cases of pneumonia admitted into King's College Hospital in 1900, and in 7 of these bronchitis was a marked feature.

In nearly all cases of pneumonia, the pleura is more or less involved in the inflammatory process, but in about 10 per cent. of the cases the *pleurisy* is so acute as to constitute a dangerous complication. In my series of 45 cases, there were 9 with well-marked pleuritic effusion. The amount of effusion may be small, but owing to the partial or complete consolidation of the lower lobe, the lung cannot collapse, and so the fluid, even if small in amount, passes upward and so may exert considerable pressure on the adjacent heart. The effusion may be serous or fibrinous, and has a great tendency to become purulent. It may develop on the opposite side of the chest,—in the year 1900 I saw four such cases. The presence of effusion, though adding somewhat to the gravity of the prognosis, in the majority of cases need not cause undue anxiety, as it generally comes on as a late manifestation, and simply renders the crisis incomplete and delays convalescence. In children the bulk of cases of *empyema* are pneumococcic in origin, and the prognosis is, as a general rule, extremely favorable, incision and drainage being followed by rapid recovery,—a result which may also often take place after mere aspiration. The fluid may, indeed, become absorbed without interference of any kind. The presence of pleuritic effusion, serous or purulent, is apt to be overlooked unless careful daily examination of the chest is made, and this course is not always advisable in the interests of the weakened patient. Its presence may be suspected if the temperature fails to come down, or if after the crisis there is a recrudescence of the pyrexia. In children this recrudescence frequently heralds the occurrence of *empyema*. Examination of the chest in the case of an adult will usually reveal diminution or absence of breath-sounds, and also of vocal fremitus and resonance at one base, while the dulness becomes much more pronounced, with a greater sense of resistance. In a child, on the other hand, and rarely also in the adult, there may be a large collection of fluid, serous or purulent, with distinct though distant tubular breathing and even whispering pectoriloquy. A striking physical sign in such cases may be the presence of tubular breathing

over a vertical strip in the lower interscapular region, with diminution or absence of breath-sounds at the extreme base. In any case of doubt the exploring-needle ought to be resorted to, though the displacement of the cardiac apex may have already confirmed the diagnosis. It is probably correct to say that the more severe the pain and the more pronounced the friction, the greater the tendency to pleuritic effusion as a complication. A policeman, aged 33, was admitted to the hospital with pneumonia of the left base. The pain in the left side was extremely severe, causing insomnia, while coarse frictions were audible over the whole infrascapular region. The crisis occurred on the seventh day, but the friction at the left base persisted. A few days later the patient became delirious, the temperature again became elevated, while the left base was found to be absolutely dull, with loss of vocal fremitus and breath-sounds. Pus was obtained on exploration; a rib was resected and the cavity drained, whereupon the patient made an excellent recovery.

Pericarditis is, without doubt, one of the gravest complications of pneumonia, and proves fatal in quite half of the cases. The involvement of the pericardium is very apt to be overlooked, especially when one remembers that in the case of left-sided pneumonia an inflammation of the pleura overlying the heart may give rise to a to-and-fro friction sound practically indistinguishable from true pericardial friction. Dr. Kingston Fowler makes the interesting and important observation that the presence of pericarditis may be suspected from the position assumed by the patient, who often prefers to be propped up with pillows instead of lying flat upon his back, as in uncomplicated cases. This orthopnea, which is often so characteristic of pericarditis with effusion, is not a symptom of uncomplicated pneumonia. Professor Welsh, of Adelaide University, believes that most of the cases of fibrinous pericarditis with seropurulent effusion are due to pneumococci, whether an antecedent pneumonia can be traced or not. Another reason for the overlooking of this complication is that the area of the pneumonic dulness may include that of the pericardial effusion. Pericarditis occurs in pneumonia in the proportion of from 0.5 to 5 per cent. of the cases, and according to Dr. Kingston Fowler is not, as is generally supposed, more frequent in cases of left-sided pneumonia.

In pericarditis, as in pleurisy, the crisis is often incomplete and the period of pyrexia prolonged. I have already mentioned

one case of this complication in speaking of the question of relapse.

Acute endocarditis, both simple and ulcerative, may occur in the course of pneumonia, though it is fortunately a rare complication. In the fatal case just alluded to, in which pneumonia was complicated with pericarditis, I found the aortic valve covered with recent vegetations.

Acute meningitis is also, fortunately, a rare but invariably fatal complication. When referring to the question of relapse, I alluded to a case in which this complication proved fatal. A culture of the pneumococcus was readily obtained from the purulent meningitic exudation.

As regards the sequels, we may mention, in the first place, *abscess of the lung*, which is a very formidable and generally fatal complication. It occurs in about 1 per cent. of all cases, and in 4 per cent. of fatal ones. When it follows inhalation pneumonia the abscess-cavity is often irregular in form with ragged shreddy walls. It may discharge through the bronchus, and may be diagnosed by a peculiar greenish purulent sputum. Occasionally, as in the case already alluded to in dealing with inhalation pneumonia, it may become encapsulated, but it is generally beyond the reach of surgical interference.

When the vessels of a portion of the lung have become blocked by thrombosis or embolism and when putrefactive bacteria are present, the serious condition known as *pulmonary gangrene* results. Its presence may be diagnosed by the breath and sputum becoming extremely offensive, and by the presence of yellow elastic tissue on microscopic examination. The fetor is so horrible that the diagnosis is usually unmistakable. Gangrene occurs in about 3 per cent. of fatal cases. Both abscess and gangrene, coming on as they do after the crisis, are often heralded by an unaccountable prostration even before the characteristic symptoms appear.

We now come to the much-debated question of the relationship between lobar pneumonia and *pulmonary tuberculosis*. It used to be the common opinion that phthisis not infrequently follows pneumonia; personally, I consider this to be a rather rare sequel. I have frequently heard it stated that when the temperature continues elevated for some weeks one ought strongly to suspect the existence of chronic pulmonary tuberculosis. Such a condition,

however, I believe to be much more frequently due to delayed resolution, pleurisy, empyema, or some such complication; still, undoubtedly tuberculosis does sometimes occur, and personally I have seen during the last few years at least four cases of basal phthisical excavation which have followed directly on an attack of lobar pneumonia. I believe that pulmonary tuberculosis is a much more common sequel of catarrhal pneumonia. During the first influenza epidemic (some twelve years ago) I was class assistant to the professor of pathology at Edinburgh University, and had the opportunity there of seeing a very large number of cases of tubercular bronchopneumonia which directly supervened on influenzal pneumonia which is so often of the bronchopneumonic type. This post-influenzal sequel has not been so commonly observed in recent years.

There is a form of acute pulmonary tuberculosis known as pneumonic phthisis or tuberculous pneumonia, in which a whole lobe, often the upper one, becomes rapidly and completely consolidated within two or three weeks or even less. I have seen two such cases. In these, however, I believe the tubercle bacillus is present from the outset, so that it cannot properly be described as a post-pneumonic sequel. In one of these cases, a middle-aged man, the diagnosis was only made on discovering the tubercle bacillus in the sputum. This case is described in the last number of the King's College Hospital Reports.

Whether chronic *fibrosis* of the lung (chronic interstitial pneumonia) occurs as a post-pneumonic sequel or not is also a question which has led to considerable discussion. I believe that a true fibrosis of the lung rarely originates in this way, though I do not deny that the pleuræ and interlobular septa may remain permanently thickened, from which ultimately fibrous processes may develop which may lead to a greater or lesser degree of pulmonary fibrosis.

Of late years, and particularly in America, it has become the custom to deny the occurrence of ante-mortem *cardiac thrombosis* as a factor of any importance in pneumonia. The older writers spoke of "clot in the heart" as the great cause of death in this disease, basing their opinion on the fact that in pneumonia more than in any other disease the ventricles were found filled with firm decolorized clot, passing into the great vessels, particularly on the right side of the heart. Of late years, Professors Welch, Osler, and others have adduced a great deal of evidence in support of the

view that this clotting is post-mortem (or occurs during the death agony) and is not ante-mortem at all. It seems to me that these observers have rushed to the opposite extreme and have probably erred in so doing. Though the great part of the decolorized clot already alluded to is no doubt due to post-mortem change, yet I believe that ante-mortem clotting does occur, and may indeed be an important factor in determining the cause of death. In fact, I would go so far as to say that the peculiar virtue of ammonium carbonate and its universal employment in the treatment of pneumonia is largely due to its value as an anti-coagulant as well as to its stimulant action on the heart. The late Sir Benjamin Ward-Richardson adduced very strong evidence in support of this theory.

A year ago I was attending a young lady, 21 years of age. The case was a typical one of pneumonic consolidation of the left lower lobe. The only noteworthy point was the high pyrexia, the temperature on two occasions reaching 106° F. The crisis occurred on the eighth day, the patient made an excellent recovery, and rapidly regained strength, while the physical signs at the left base quickly disappeared. A fortnight after the crisis, when the patient was practically convalescent, I was hastily summoned to see her, and found her sitting up in bed, gasping for breath, with marked orthopnea and an extreme degree of cyanosis; the pulse was scarcely perceptible at the wrist. Half an hour before my arrival, the patient had been sitting up having breakfast, feeling quite well and conversing with her nurse, when suddenly the condition I have just described came on. Brandy was administered before my arrival. The suddenness of the onset, the orthopnea, cyanosis, and feebleness of the heart's action, taken in conjunction with the absence of evidence of cardiac dilatation or lung involvement, induced me to conclude that she was suffering from cardiac thrombosis, and that a portion of the clot had become detached and was probably impinging against the origin of the pulmonary artery. I immediately held a consultation with one of the senior physicians of the London Hospital. He corroborated my opinion, and stated that the patient was undoubtedly suffering from right-sided cardiac thrombosis, and expressed his belief that the girl was dying and would probably not live more than a few hours. This result was happily not realized, and although she hovered between life and death for the next week or ten days, yet by means of strychnin injections, large doses of

ammonium carbonate, and brandy, she was with difficulty pulled through and ultimately made a perfect recovery, being now well and strong. That the diagnosis was correct was proved three days after the sudden onset by the occurrence of hemoptysis, and the physical sign of a pulmonary infarct in the left inframammary region. Personally, I believe that during the course of the high pyrexia ante-mortem clotting had occurred in the right auricle or its appendix, or possibly at the apex of the right ventricle, and that it had not been entirely absorbed even a fortnight after the crisis.

Before concluding, I should like to say a few words regarding pneumonia in *children*. I have already alluded to the absence of sputum and the frequent absence of crepitations. There is a considerable divergence of opinion regarding the pathologic type of pneumonia found in children. Some authorities go so far as to say that 75 per cent. of such pneumonias are of the bronchopneumonic type, while, on the other hand, in a recent paper read at one of the meetings of the British Medical Association (1900) Dr. Tirard showed from the analysis of a large number of cases at the Evelina Hospital for Sick Children that after the age of three there was almost a preponderance of lobar pneumonias, with a tendency to engorgement of other portions of the lung. Be this as it may, all observers are now agreed that in both types the pneumococcus is by far the most important causal agent, even in those cases following measles and whooping-cough. The temperature may be of a remittent type, there may be erythema with redness of the fauces, while cerebral symptoms are apt in some cases to mask those of the pneumonia proper. Professor Osler, indeed, speaks of a "cerebral" pneumonia in children, in which the disease closely resembles meningitis, and is characterized by marked cerebral symptoms, delirium, high remittent pyrexia, irritability, muscular tremor, and even retraction of the head and neck, and may be ushered in by convulsions. These symptoms, taken in conjunction with the frequent absence of crepitations, sometimes leave us in doubt as to what is the actual condition present. We do not, however, have the meningitic cry, the curled-up attitude, the retracted abdomen, the photophobia or strabismus, and but rarely the vomiting and opisthotonos.

It is possible that the gastro-intestinal symptoms met with in children may be partly due to the swallowing of the sputum. The

prognosis in children, in the case of lobar pneumonia, is extremely favorable, and even the apical cases as a rule do remarkably well.

In children I have seen the process of resolution delayed for many weeks, suggesting the strong probability of pulmonary tuberculosis, and yet the cases ultimately clear up completely. This condition, however, is commoner in cases of bronchopneumonia. In those cases in which the bronchopneumonic process is extensive and the patches confluent, leading to consolidation of a considerable portion of a lobe, the diagnosis between lobar and bronchopneumonia in children is extremely difficult, though the bronchopneumonic variety may often be recognized owing to the presence of pre-existing measles or whooping-cough, by its more gradual onset, more prolonged course, and remittent pyrexia. The mortality is much higher than in lobar pneumonia, which in healthy children rarely proves fatal.

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SUDDEN DEATH DUE TO RESPIRATORY DISORDER

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Of Philadelphia

It must be confessed that many sudden deaths are attributed to wrong causes. This is frequently owing to a lack of opportunity to make a post-mortem examination, and, perhaps, quite as often to our intuitive belief that many sudden deaths are brought about either through heart failure (whatever that may mean) or brain disease. On the other hand, in many cases it is too true that even in the light of a post-mortem investigation the cause of death remains shrouded in mystery. This is well demonstrated in the following example which furnishes the inspiration of this paper.

Eleven years ago (September 11, 1892), F., a clerk, came under my care with an aortic lesion, and frequent attacks of genuine angina pectoris, from which he said he had suffered for more than a year. The anginal attacks, which came on quite frequently, and recently more severely, were very much ameliorated by the administration of strychnin in large doses by the mouth and hypodermically. He was able to continue his vocation, and on the evening of November 8 of the same year—the day of the Presidential election—F., who was a very ardent Democrat, went down town with his wife to hear the election returns. Late in the evening he was quite elated at hearing that his candidate was successful, then returned to his home in the horse-cars and arrived there shortly after midnight. He went to bed feeling as he had felt for some time, and after being in the recumbent position for about twenty minutes, suddenly jumped out of bed and fell over dead in a few minutes. There was no hemoptysis.

Post-mortem examination, eighteen hours after death, revealed pleural adhesion of the right lung. The two lower lobes of the right lung were in a state of deep red congestion, and the upper lobe of the same side in a condition resembling dark red hepatization, although sections of this did not sink in water. The left lung was

deeply congested. There was oozing of serous fluid from the incised surface of the right lung, and also from the cut bronchial tubes. The heart weighed two pounds. The left ventricle was hypertrophied, and the wall of the right ventricle thin and contained several mushy spots of fatty degeneration, which crushed between the fingers, but there was no break in its continuity. There were no ossified coronary arteries, but the aortic valves were diseased.

Viewed from a stand-point of its clinical history, physical signs, and sudden termination, one would naturally come to the conclusion that the cause of death in this case was either an attack of angina pectoris or rupture of the heart walls. Yet the post-mortem findings absolutely negated this opinion, and make it quite clear that the cause of death came from the direction of the respiratory organs, and not from the heart. Another deduction is also very palpable, and that is that the pulmonary lesions found post-mortem in all probability developed very suddenly and during the last few minutes of his life. These could hardly have existed when he reached home, or even immediately after he had gone to bed, for he experienced no new inconvenience, and felt as well as he had for some time.

After all the elucidation which these points apparently afford, it is evident that we are still far from disclosing the cause of this patient's death. What was the reason for the sudden pulmonary engorgement? Did the cause of death operate from a number of different centers, or from only one? May the lungs in a few minutes become so thoroughly engorged with blood as to give them the appearance of pneumonic infiltration? May a person appear to be practically well so far as performing the practical affairs of life is concerned, and in the midst of this condition be fatally attacked with pulmonary embarrassment? There is little doubt that sudden changes of this character are oftener a cause of death than we are, perhaps, willing to admit, because their intimate pathology is not clearly defined as yet. It is well known, however, that so far as the lungs go the disorder consists essentially of a sudden and extensive exhalation of blood into the lung tissue, giving rise to a pulmonary engorgement without any or much extravasation of blood into the bronchial tubes. It is not a hemoptysis, but an apoplexy of the lung, although it is probable that both of these affections have a common organic basis.

This opinion of the apoplectic character of this affection is almost entirely confirmed by Dr. Hornhardt in a paper on sudden death through pneumonia in the apparently healthy. This author collected 59 cases of sudden death due to pneumonia from the necropsy records of the Pathologic Institute in Kiel, covering a period from 1873 to 1896. All these individuals died suddenly, and without having complained of any illness or even indisposition, or without any evidence of illness detected by their friends, or persons who were with them. In 24 cases death took place very suddenly while they were employed on the street. In the others, death took place before they were reached by physicians. In 13 of 41 adult cases, alcoholism was strongly suspected on account of the chronic hydrocephalus, meningitis, etc., which were present. Out of the 41 adults, in 9.7 per cent. the lungs were in a state of red hepatization; in 58 per cent., in a state of gray hepatization; in 2.4 per cent., in a state of yellow hepatization; and in 17 per cent., in a state of puriform softening.

The pulmonary pathology of this disease is made tolerably clear by the above data. It is obvious, however, that its morbid anatomy extends farther than the lungs, and that, for reasons which will presently appear, there is a strong suspicion that the respiratory centers are involved in this morbid process. When we reflect that pulmonary engorgement, hemoptysis, and acute pneumonia are frequently caused by brain injuries, as the following examples will show, there is no escape from this position. Nothnagel¹ scratched the upper brain surface of rabbits with a needle and produced intense infiltration of blood throughout the whole extent of their lungs. Fleischmann² says that in his vivisection work on the brains of dogs and guinea-pigs his attention was drawn to the fact that the most common cause of death among his animals was pneumonia, that compression or incision of the pons was almost constantly followed by ecchymosis of the pleura and apoplexy of the lungs, and that if only half of the pons was injured the ecchymosis occurred in the opposite lung. Falk³ states that the lung changes after vagotomy, which Schiff and von Wittich explain as a neuro-paralytic

¹ Centralblatt f. d. med. Wis., 1874, p. 209.

² Jahrb. f. Kinderheilkunde, 1871, iv, 283.

³ Vierteljahrsschrift f. d. gerichtliche Medicin, 1876, xxv, 269.

hyperemia of the lungs, reminded him of an acute, not a hypostatic pneumonia. Dr. Rochs contributes an article on "Injuries to the Head associated with Pneumonia from a Medico-Legal Stand-Point,"¹ in which he reports ten cases of skull fracture, nine of which were followed by croupous pneumonia, and one by double pulmonary edema, in from three days to two weeks. Falk² reports the following case: A woman, aged 27 years, in good health, was shot in the left temple in a cemetery at two o'clock in the morning. At one P.M. she was found and brought to the hospital in a state of unconsciousness, from which she never recovered. Her pulse was 63, respiration 26, and temperature 37° C., and there was prolonged expiration over both lungs. In the evening of the same day she had convulsions and vomiting, and death ensued on the following morning. The necropsy revealed the right lung to be dark red, to sink in water, and from its cut surfaces oozed brown-red viscid fluid. The branches of the pulmonary artery were empty, and the larger bronchi contained froth. The left lung was edematous throughout. Dr. Falk says that the lung condition in this case is similar to that which is described by Rokitsky as inflammatory engorgement, and by Laennec as engorgement, both denoting the early stage of croupous pneumonia. It is a well-known fact that the lungs of the insane like those of persons who suffer from cranial injuries are also frequently extravasated with blood, as the following examples given by Jehn,³ in an article on extensive capillary diffusion of bright-red blood in the pulmonary tissue of the insane, well show (melancholia and mania, each one case, and paralysis three cases). He found extravasation of bright-red blood in both lungs. In some lungs the bloody areas were scattered, and in others large spaces were involved. The bronchi were empty, and no blood could be pressed from either the lung surface or bronchi. Pieces of lung floated just beneath the surface of the water. The red discoloration of the lungs was uniform, and the areas which were free from extravasation were edematous, and comprised pneumonic deposits. Microscopically the alveoli, without exception, were filled with red blood-corpuscles, but there was no change observable

¹ Vierteljahrsschrift f. gerichtliche Medicin, 1887, xlvii, 12.

² Ibid., p. 292.

³ Centralblatt f. d. med. Wissenschaften, 1874, p. 340.

in the blood-vessels or lung tissue. During life there was no manifestation of lung disease.

It is evident, therefore, that pulmonary apoplexy, or sudden pulmonary engorgement, is a problem that must be solved from its nervous and not from its pulmonary side. Even from an *a priori* stand-point, the suddenness of the onset, its extensiveness, and the uniformity of its behavior point out most forcibly that the fatal influence which is at work emanates from a single source, and also that that source is probably of a nervous nature. But with the corroboration of the many instances of sequential relationship between injury of the brain and pulmonary infiltration, it becomes clear enough that the mechanism at the foundation of this affection is neurotic and not pulmonic.

ON THE OCCURRENCE OF A FORM OF LEUKEMIA INTERMEDIATE IN TYPE BETWEEN THE LYM- PHATIC AND THE SPLENOMEDULLARY FORMS, WITH NOTES OF A CASE IN A CHILD OF FIVE YEARS

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UNTIL a few years ago the absolute dissimilarity of the two types of leukemia—the lymphatic and the splenomedullary—and the non-existence, or even the impossibility, either of a mixed type or of the passage of the one form into the other, was regarded as one of the best proven dicta of medicine, and the fact that in practice, cases, almost without exception, fall into one or other of these classes, cannot but continue to render this classification clinically the most convenient at our disposal. The great weight of Ehrlich's authority, to whom modern hematology owes its birth, is of course on the side of current opinion,—it is, indeed, his and his pupils' researches which have afforded a rational basis for the separation of the two forms of the disease. But quite recently a certain amount of work has appeared which has tended to show that the separation of the two varieties of leukocytes, and therefore of the two types of leukemia, is less definite than has hitherto been supposed, and it is as a contribution to this aspect of the subject that the following paper is offered.

It will be remembered that according to Ehrlich's teaching there are two totally distinct varieties of white blood-cells—the lymphocytes and the cells of the bone marrow, or granulocytes. (The last term, though convenient, is not, as we shall see, strictly accurate, since some of the cells of the marrow have no granules.) These two sets of cells differ from one another, (1) in their source, the former arising from the lymphatic tissues, the latter from the bone marrow, and the one never develops into the other, nor have they a common ancestor. (2) They differ morphologically in that the former have usually a rounded nucleus, and a non-granular protoplasmic body

more strongly basophilic than the nucleus, while the latter have irregular or rounded nuclei, and contain granules which are either acidophilic, neutrophilic, or basophilic. Among the granulocytes, however, we must also reckon a cell of the bone marrow which has no granules, and which probably develops into the "transitional" leukocyte—the non-granular mononuclear. It differs from the lymphocyte in having a relatively smaller nucleus, while *its protoplasm is less strongly basophilic than its nucleus*. (3) The lymphocytes differ from the granulocytes in yet a third respect: they are incapable of ameboid movement, and therefore of active passage through the capillary wall and into the circulation, and in view of the absence of granules they cannot possess that secretory activity of which Ehrlich regards the granules of the other group of cells as an evidence. The granulocytes, on the other hand, show an ameboid movement, and are therefore capable of emigration from the vessels.

Such, in brief, is the general theory of the leukocytes, and from it it naturally follows that lymphatic and splenomedullary leukemia are two totally distinct pathological conditions, the former being due to an increased activity of lymphatic tissue, with passive extrusion of the newly-formed cells into the blood, while the latter is regarded by Ehrlich as caused by a specific agency of unknown nature exerting a positive chemotactic influence on the cells of the marrow. We know that not only does such chemotaxis take place, but that specific toxins evoke specific reactions on the part of the marrow. Thus most bacterial toxins produce a leukocytosis in which neutrophilic cells take part; other less known products (possibly the results of epithelial destruction in the body), eosinophilia, and in rarer cases still we get a basophilic leukocytosis. There is thus every reason from analogy to suppose that splenomedullary leukemia may be brought about in a similar way.

Much as this theory has to commend it, certain objections to it are not wanting, and these must be referred to. Many observers have not subscribed to the view that the lymphocytes and granulocytes are genetically distinct, and to name only one, Gulland¹ derives all the leukocytes from a common ancestor. The cell which has given rise to most difficulty is the non-granular mononuclear, which all writers, Da Costa, for example, agree is difficult to distin-

¹ Journal of Physiology, xix, 1896.

guish in ordinary film preparations. Michaelis and Wolff¹ have recently tried to show that, in addition to the lymphocyte, a cell called by them a "lymphoid cell" exists (apparently corresponding exactly with Ehrlich's non-granular mononuclear), which may either develop granules in its cell body, or, its protoplasm becoming strongly basophilic, be transformed into a lymphocyte. By special methods these observers have also demonstrated granules in the lymphocyte and in the non-granular mononuclear,—granules which differ somewhat from those generally recognized, it is true, but still apparently of similar nature. The possibility of an active lymphocytosis as against a passive one seems clearly proved by the indisputable occurrence of lymphocytosis in the early stages of tubercular pleural effusions, while Hirschfeld² states that he has made out ameboid movements in the lymphocytes in a case of lymphatic leukemia. If, then, the above distinctions between the lymphocytes and the granulocytes are less absolute than we have been led to think, it seems extremely probable that the same may be the case with regard to leukemia, and, as a matter of fact, a certain number of intermediate cases have been reported. Before these are discussed, however, the notes of a case which forms the text of this communication may be given:

Mary W., aged five years, was admitted to the Hospital for Sick Children, Edinburgh, under the care of Dr. John Thomson (whom I have to thank for permission to record the case), on October 9, 1902, with the complaint of swelling in the abdomen and weakness, of about one month's duration. The patient was the fifth child of a family of seven, born of healthy parents, and there is nothing noteworthy in her family history. She has had measles, whooping-cough, and chicken-pox, and about two months ago suffered from sore throat and enlargement of the cervical glands, on account of which she was confined to bed for a month. Since then she has been weak and bloodless, has lost her appetite, but complains of no pain. A month ago, as the mother was bathing the child, she noticed a hard swelling in the abdomen, which has remained ever since. No other symptoms beyond weakness, loss of appetite, and a transient attack of swelling about the eyes have been noticed. No

¹ Deutsche med. Woch., 1901.

² Berliner klin. Woch., 1901.

hemorrhages have occurred, nor were any observed during the subsequent course of the patient's illness.

On admission the child was well developed and nourished, but obviously anemic. A crusted eruption surrounds the mouth. There is marked edema of the soft tissues in the region of the right orbit, and to a less extent on the left side. No cutaneous hemorrhages are present. The patient habitually breathes through the mouth, the tonsils are enlarged, and the nostrils are narrow. The temperature is 100° F., the pulse 110. A deep horizontal sulcus runs transversely across the lower part of the anterior aspect of the thorax; the respiratory system is otherwise normal.

The abdomen is distended and has some dilated veins running over its surface. On palpation the spleen and liver are enlarged, the former filling more than half the abdomen, and reaching slightly across the middle line at the level of the umbilicus, and extending down to within an inch of Poupart's ligament. The liver dulness extends from the third rib in the nipple line to one and one-half inches below the costal margin. The other abdominal organs and the digestive functions seem normal.

Nearly all the superficial glands—submaxillary and submental, anterior and posterior cervical, subclavicular, femoral, and inguinal—are slightly enlarged and hard. There is no tenderness over the bones. There is a little dulness over the manubrium sterni, and extending about one inch to the left of that bone, which is probably due to an enlarged thymus.

The circulatory system is normal, except for a soft functional apical bruit. The urine is normal; the amount of uric acid was not estimated, but no deposit was ever present. The fundi oculi were examined by Dr. Argyll Robertson, who reported that in the right eye the vessels were distended and tortuous, and there was probably incipient retinitis. The left eye was normal.

The patient remained in hospital for about four weeks, her condition altering very little during that time. The temperature was occasionally and irregularly pyrexial; never, however, rising above 100.4° F. She was taken home to the country at her parents' desire, and died about six weeks later. Unfortunately, there was no post-mortem.

The blood was examined several times during her stay in the hos-

pital, and once after her return home. As the subjoined Table II shows, it did not vary greatly from time to time (see page 223).

The recorded cases bearing on the possible occurrence of intermediate form of leukemia fall into two categories: (1) Those which from being lymphocytic underwent change to the myelocytic form, or *vice versa*; and (2) those which simultaneously presented features of both varieties.

To the first group must be referred the case reported by Hirschlaff,¹ which, running its course as an ordinary lymphatic leukemia, showed toward the end a number of granular leukocytes in the blood. In all probability, as Ehrlich pointed out in discussing it, this was an instance of an ordinary leukocytosis taking place in a case of lymphatic leukemia—an occurrence which is not unknown. Van der Wey² describes a case of splenomedullary leukemia which ended fatally with acute symptoms; and, simultaneously with the development of these, the neutrophilic myelocytes, polynuclears, and eosinophiles diminished, while numbers of large non-granular mononuclear cells (Fraenkel's large lymphocytes) appeared in the blood. Ehrlich explains this as due to the disappearance of the granules in the myelocytes on account of inanition; but on reading Van der Wey's description, one cannot put aside the idea that the change was really such as he suggests, and this view of the case is the one accepted by Fraenkel,³ who uses it to support his opinion that in acute leukemia the blood change almost invariably consists in an excess of large lymphocytes. Seelig's⁴ case of conversion of the myelocytic into the lymphatic form was almost certainly a lymphatic one from its commencement, as the large mononuclear cells seen during life are said to have contained no granules, and were probably large lymphocytes, not, as Seelig thought, myelocytes. Walz,⁵ in a review of the literature, states that no conclusive case of transformation of one into the other type has been reported; in my own opinion, Van der Wey's case is the only one pointing in this direction.

As to the second group of cases, Bloch and Hirschfeld's⁶ case

¹ Centralblatt f. innere Med., 1898, p. 836.

² Arch. f. klin. Med., lvii, 287.

³ Verhandlungen d. XV Congresses f. innere Med., Wiesbaden, 1897, p. 359.

⁴ Arch. f. klin. Med., 1895, liv, 537.

⁵ Centralbl. f. allg. Path., 1901, xii, 967.

⁶ Ztschr. f. klin. Med., 1900, xxxix, 32.

of "lymphatic myelogenous leukemia" is frequently quoted. It occurred in a rachitic infant, eight months old, the proportion of white to red cells being as 1 to 12, and the differential count showing the following percentages: Small lymphocytes, 27.14; large lymphocytes, 33.8; polynuclear leukocytes, 28.8; neutrophilic myelocytes, 10.26. Isolated eosinophiles and "mast"-cells were also present, and numerous megaloblasts and normoblasts were found. This case is undoubtedly one of pseudoleukemic anemia, or splenic anemia of infancy, and not of true leukemia at all. The proportion of myelocytes is not higher than is often met with in the former disease, and the clinical history, as well as the blood changes and the results of the pathologic examination, put the diagnosis practically beyond question.

Michaelis's case¹ is of great interest in this connection. The patient was a woman, aged 50 years, with great enlargement of the spleen and progressive anemia of three months' duration. No hemorrhages occurred. The blood examination showed 3,450,000 red corpuscles and 16,000 leukocytes, with the following differential count: Small lymphocytes, 20; large lymphocytes, 56; polynuclears, 16; myelocytes, 7.2; eosinophiles, 0.4; mast-cells, 0.4. Normoblasts were at first present in increasing numbers, but disappeared altogether latterly. On post-mortem examination, the spleen and bone marrow were found packed with lymphocytes and giant cells with irregular nuclei, myelocytes being few; similar giant cells were also found in the liver and glands. The neutrophilic myelocytes in the blood were closely related to the lymphoid cells described by Michaelis and Wolff (vide supra) as the common ancestor of all leukocytes, their protoplasmic bodies being small and their granules scanty. The observer regards this appearance as due to incomplete differentiation of the indifferent lymphoid cell. He looks on the case as one of leukemia in which these lymphoid cells proliferated, giving rise on the one hand to lymphocytes and on the other to myelocytes—imperfectly developed, it is true, but yet differentiated to the greatest extent of which the lymphoid cells were capable.

Wolff² describes the blood of two cases (the clinical details of which are not given) as follows:

¹ *Ztschr. f. klin. Med.*, xlv, 1902, p. 87.

² *Ibid.*, xlv, 1902, p. 411.

	CASE I.	CASE II.
Proportion of whites to reds.....	1 to 4	1 to 10
Small lymphocytes.....	5.85	9.33
Large lymphocytes.....	72.14	69.09
Lymphoid cells.....	16.7	4.67
Polynuclears.....	3.14	9.33
Myelocytes.....	1.29	4.75
Eosinophiles.....	0.72	1.5
Mast-cells.....	0.15	1.33

The cells classed under the head of lymphoid cells showed (with Michaelis's eosin-methylene-blue-acetone stain ¹) all stages of transition between myelocytes and lymphocytes—some having a slightly basophilic protoplasm, others fine bluish granules, and others, again, purplish granules like those of the myelocytes. Many of the large lymphocytes merged insensibly into this group by reason of the faintly basophilic character of their protoplasm. The second of Wolff's cases, at least, can scarcely be dismissed as lymphatic leukemia without consideration; and it would rather seem to be a genuine intermediate type, even if we cannot subscribe to Wolff's theory and call it a "lymphoid-cell leukemia."

To revert to my own case, which falls into the group we now are considering. The state of the blood is shown in the following table. The changes in the red cells call for little note; there was some poikilocytosis, normoblasts were numerous, and in not a few instances mitoses either in these or in the white cells were present.

	OCT. 11.	OCT. 14.	OCT. 23.	NOV. 11.	NOV. 29.
Number of red corpuscles	2,200,000	2,700,000	2,610,000	2,700,000
Number of white corpuscles.....	240,000	257,000	240,800	240,000
Small lymphocytes.....	13	7.4	10.2	8	8.2
Large lymphocytes.....	32	33.4	34.4	46.5	56.4
Non-granular mononuclear "lymphoid cells"		16.6	15.9		
Polynuclears.....	18	21.8	16.3	22	17.2
Myelocytes.....	27	15.5	17	15.8	12.1
Eosinophiles.....	2.6	.6	.8	1.5	1
Eosinophilic myelocytes.....	3.4	1.3	1.1	1.8	.7
Mast-cells.....	3	3.4	4.3	4.4	4.4
Nucleated reds per c.mm.	7,200	6,700	4,000	7,700

¹ I cannot too strongly commend the use of this stain in addition to the ordinary triacid mixture. It enables one in a single film to differentiate all the forms of granulation, including the basophilic, and is a much better stain for the lymphocytes than the triacid mixtures.

The differential count shows that it is certainly not a case of lymphatic leukemia; the large proportion of myelocytes, the absolute increase of eosinophiles, and the abnormal number of mast-cells are characteristic of the splenomedullary type of leukemia, and are found together in no other disease. On the other hand, we also have evidence of an excessive production of lymphocytes, which ought not to occur in splenomedullary leukemia. In Cabot's series of cases of that disease, for instance, one has 26.5 per cent. of large lymphocytes, and another 14.5 per cent.; but these are exceptional, and the average is only 4.6 per cent. In Da Costa's series the average is 8.1 per cent., the maximum 18 per cent. It should also be noted that these writers make no distinction between large mononuclears and lymphocytes, so that their figures must be compared with the sum of both these cells in my differential counts. In fact, adding together all the non-granular cells in my case, we get percentages as high as 64 and 67, numbers which, taken with the high total leukocyte count, would point strongly to lymphatic leukemia, were it not for the presence of myelocytes and mast-cells. I found the same intermediate forms as Wolff describes. While with the triacid stain all the cells under the first three heads were tinged alike a bluish green of varying intensity, Michaelis's stain enabled me, as a rule, to differentiate the typical lymphocyte from the lymphoid cells. But these latter in some cases showed (*a*) a protoplasmic body almost as deeply basophilic as that of the lymphocyte, and (*b*) indications of fine granules resembling basophiles or myelocytes, yet insufficient to place the cells in either of these categories. On the whole, however, the lymphoid cells approximating to the lymphocytes were much more numerous than those resembling the granulocytes. None of these intermediate types of cell resembled Türk's "*reizungsform*"; the triacid mixture stained them all pale blue, not brown.

I cannot but think that, whether we accept Ehrlich's division of the white cells of the blood or not, this case must be interpreted as one in which all the leukocytes have undergone increase—that is, *it is intermediate between a lymphatic and a splenomedullary case*. It seems strongly to support the idea that these uninuclear non-granular lymphoid cells are the common ancestors of the other leukocytes.

As a further example of the association of myelocytes with a lymphemic condition of the blood, I may instance a case of chloroma which I saw at the Sick Children's Hospital about 18 months ago. The differential counts are as follows:

	Oct. 5.	Oct. 15.	Oct. 29.	Nov. 11.
Total leukocytes.....	25,000	29,000	61,000	64,000
Small lymphocytes.....	15	19.4	19.3	15.5
Large lymphocytes.....	48.5	48	51	53.5
Polynuclear leukocytes.....	31.5	28.6	16.7	16
Eosinophiles.....	few	few
Myelocytes.....	5	4	12.6	15

I was not at this time familiar with Michaelis's stain, and the triacid did not, of course, differentiate the large lymphocytes from the non-granular mononuclears. I am not aware that such a condition of the blood has hitherto been described in chloroma, but the disease is rare, and the blood has very seldom been carefully examined. It appears usually to resemble that in lymphatic leukemia. The case is reported as additional evidence that myelocytes in considerable numbers may occur in conjunction with a lymphemia—a fact which still further tends to break down the idea that myelocythemia and lymphemia are mutually exclusive.¹

In conclusion, it may be pointed out that this is one of the youngest patients in whom leukemia not of the lymphatic type has been observed. The only other patients under ten years of age are Baginsky's,² a girl of nine, and a doubtful case of my own.³ Wolff very justly remarks that in the attempt to establish the existence of an intermediate form of leukemia, a case in a child is to be regarded with suspicion, on account of the possibility of confusion with pseudoleukemic anemia. My patient was much beyond the age at which this disease occurs, and the high leukocyte count is also conclusive against it. Baginsky's patient showed a leukocytosis of 410,000, with 56.7 per cent. myelocytes, 36.1 per cent. polynuclears, and 4.1 per cent. eosinophiles—nothing in any way comparable with the present case. Every one is aware that in childhood lymphocytosis is common; I cannot, however, think that the patient's age explains the peculiarities of this case. It is one of very considerable interest, and is offered in elucidation of a somewhat obscure question.

¹ Reported in the *Brit. Med. Jour.*, vol. i, 1902, by Dr. Melville Dunlop, under whose care the patient was, and by whose kindness I was allowed to examine the blood, and am now able to record it.

² *Festschrift f. Jacobi*, 1900.

³ Referred to in *INTERNATIONAL CLINICS*, Eleventh Series, vol. ii.

CLINICAL EVIDENCES OF MYOCARDIAL DAMAGE IN RHEUMATIC FEVER

BEING LECTURE II OF A SERIES OF CLINICAL LECTURES ON RHEUMATIC FEVER
DELIVERED AT THE HOSPITAL FOR SICK CHILDREN, GREAT
ORMOND STREET, LONDON

BY F. J. POYNTON, M.D., F.R.C.P. LOND.

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LADIES AND GENTLEMEN: This demonstration is the second of three which I hope to give upon the subject of rheumatic fever. In the first one I considered endocarditis as a symptom of infective diseases, dealing especially with rheumatic endocarditis. To-day I am considering the part taken by the myocardium in rheumatic heart disease. In the future I hope to deal with the clinical analogy between the various rheumatic lesions.

I

The aim of the first demonstration was to show by means of clinical cases and experimental evidence how clear a conception of rheumatic endocarditis can be obtained by the acceptance of the infective nature of rheumatic fever. We can trace the entire process in our thoughts, picture it in our minds, and talk of it in plain and simple language. There are, I admit, some difficult questions connected with malignant endocarditis, but even these become less obscure when rheumatic fever is thus studied. To-day I have a more difficult task, but the subject is so important that if I only succeed in making clear the reasoning upon which its study is based, I shall have given you some assistance.

We have to consider the damage to the cardiac wall that may result from one or repeated attacks of rheumatic fever. As in my former lecture upon endocarditis, I shall endeavor to deal with this question clinically and to apply it practically, and although I must approach it from theoretical and pathological stand-points, my hope

is to leave it in such a position that its clinical importance will be manifest.

If we consider the human heart, quite apart from the lessons of disease, we cannot but think that its healthy function depends more upon the soundness of the cardiac muscle, than upon the integrity of the valves and pericardium. A study of heart disease strengthens us in this opinion, for although the valves may be much damaged by disease, we repeatedly see the cardiac wall come to the rescue, and although the pericardium may have become functionless from general adhesion, yet may life be preserved for years, and death eventually result from a totally different cause.

It may then seem strange that only of late has it been thoroughly recognized how important must be the condition of the cardiac wall in the very disease which above all damages the heart—rheumatic fever. We have heard a vast deal about endocarditis and pericarditis, but in proportion very little about the myocardium in rheumatic fever.

But the reason is not far to seek, and when it is recognized how much dependence is placed upon the stethoscope in the clinical detection of heart disease it becomes apparent. As a general rule the diagnosis of endocarditis without the evidence of a cardiac bruit is insecure, although there are, no doubt, some cases of advanced valvular disease, as, for example, advanced aortic regurgitation, which may be detected without a stethoscope and with absolute certainty. So, again, with pericarditis. In the absence of any pericardial friction sound it needs all the skill of the clinician to diagnose pericarditis. The stethoscope, then, is of immense value, but its very usefulness has brought with it this drawback,—a tendency to follow a process of false reasoning, which argues, unconsciously, I admit, that when there is no unusual sound heard with the stethoscope there is nothing much the matter with the heart.

Disease of the myocardium gives rise to no characteristic bruit, and often enough we are obliged to judge of its existence from the symptoms rather than by the physical signs. This is true when there is damage to the myocardium alone, but when, as in rheumatic fever, we have often to deal with a concurrent pericarditis or endocarditis, you can quite well understand how difficult it is to get any clear notion of the part taken by the cardiac wall. It is then this absence of definite physical signs which has made

the detection of myocardial disease so difficult, and the bruits and pericardial friction sounds of rheumatic heart disease have added to this difficulty by diverting attention from it.

But do not let me give you the impression that damage to the myocardium in rheumatic fever has been altogether overlooked at the bedside. That would be a false impression. About 1870 one of the greatest of our English physicians, Sir William Gull, was in the habit of pointing out, in the wards at Guy's Hospital, that acute rheumatic pericarditis was liable to give rise to a rapid dilatation of the heart which was mistaken for pericardial effusion. His opinion was quoted by Dr. James Goodhart, in 1879, when he showed at the Pathological Society of London the heart of a youth, aged 17, who had died from rheumatic pericarditis, with endocarditis. The heart was dilated and there was no pericardial effusion, but only a soft fibrino-cellular coating of exudation. In 1882 Dr. Samuel West showed the same condition of dilatation and demonstrated fatty degeneration of the muscle. Again, in Dr. A. E. Sansom's writings, we find allusions to the swollen heart of rheumatic fever. There are other scattered observations to be found, but I believe I am correct in saying that the real importance of these observations was not realized, and, indeed, they were, generally speaking, unknown.

It is to Dr. D. B. Lees that we chiefly owe the establishment of the clinical value of this condition of dilatation in rheumatic fever, and for ten years he has been upholding its importance with unshaken faith. In 1896 Dr. John Broadbent, in a monograph on adherent pericardium, from clinical observations at the hospital, brought forward important evidence in support of this view. In 1897 I had the honor of working with Dr. Lees upon the subject, and in two papers read before the Royal Medico-Chirurgical Society, in 1898, we were able to put the matter beyond the stage of controversy; while Dr. Theodore Fisher, of Clifton, arrived at the same goal independently.

To state our conclusions with the greatest brevity, we held that dilatation might occur independently of endocarditis or pericarditis, that it might be the first sign of rheumatic heart disease, and that when it occurred with pericarditis and endocarditis it was not entirely a result of those inflammations, but a result of the rheumatic poisoning. In those days we did not recognize the microbic excitant of rheumatic fever.

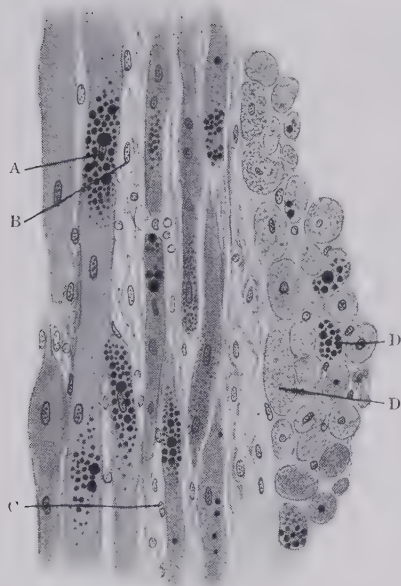


FIG. 1.—A section through the left ventricle of the heart, from a case of diphtheritic paralysis. A, fatty change; B, a muscle fiber almost destroyed; C, a muscle fiber destroyed all but the nucleus; D, damaged muscle in transverse section. (Osmic acid preparation.)

So much for the clinical history of the condition. But are there any pathological changes in the myocardium to explain these clinical observations of dilatation of the heart?

It has long been known that in cases of rheumatic pericarditis fatty changes are found in the muscle under the inflamed membrane. There have been also scattered observations upon more diffuse myocardial changes, but they are scanty, and in most cases these changes have been interpreted as secondary to endocarditis or pericarditis, and no especial attention has been directed to them.

At this point let me ask you to divert your attention for a short time from rheumatic fever to diphtheria, for the latter will assist us considerably in the study of the pathology of the myocardium. Diphtheria, we know, only too well, often damages the heart; not, as a rule, by causing endocarditis or pericarditis, but by damaging the nerve endings and muscle. In this disease we can then get an insight into myocardial affections unaccompanied by endocarditis or pericarditis.

After an attack of diphtheria death may sometimes occur with dreadful suddenness, or there may be a more gradual cardiac failure—part of a paralysis more or less general. In passing I may say that in this hospital it is remarkable how rarely we find patients who die suddenly without some warning or other, and there is almost invariably a certain amount of cardiac dilatation.

Now, diphtheria is an infective disease, just as is rheumatism, though differing in its contagious character, and in the distribution of the lesions. It is, then, of especial interest to us to know what the pathological changes are in the cardiac muscle, and the light thrown upon diseases of the heart wall by those who have investigated the myocardium in diphtheria has, I think, been very great, and their investigations most suggestive.

This drawing (Fig. 1), which was made from a section of the heart wall of a case of fatal diphtheria that I investigated in 1899, illustrates some of the changes which result and which have been for many years well recognized. The fatty changes, the nuclear changes, the alteration in the shape and size of the muscle fibers can all be seen in this drawing.

From it, I think, you will get some notion of the action of a bacterial toxin on the cardiac wall, and be prepared to hear of the changes that take place in rheumatic fever, which is also an in-

fective disease that frequently damages the heart and often causes dilatation.

In 1895 Neill and Barjon¹ gave a detailed account of the myocardium in a case of rheumatic myocarditis. In 1898 I brought before the Royal Medico-Chirurgical Society a paper upon the subject of rheumatic damage to the cardiac wall which was based upon a study of 4 cases, and in 1900 I had investigated 18 cases of acute rheumatic carditis, and Dr. Fisher, of Clifton, had investigated cases of chronic rheumatic carditis.

Later in 1900 Dr. Paine and myself were enabled to add a further link by the production of myocardial changes of a fatty nature in the hearts of rabbits injected with a diplococcus which we believed to be a cause of the disease. These pathological observations can now be put side by side with the clinical ones.

I will give only a very brief description of them and under two headings: (1) those affecting the cardiac muscle, and (2) those affecting the blood-vessels and interstitial tissues of the heart wall.

Under the changes affecting the heart muscle come (*a*) fatty changes in the muscular fibers, not only close under the pericardium, but also scattered throughout the heart wall, more especially in the neighborhood of the minute blood-vessels (Fig. 2). These changes may be slight or severe, but, in my experience, there is seldom the destruction of the muscle fibers which is found in diphtheria. (*b*) Loss of striation, exaggeration of striation, and segmentation. And (*c*) nuclear change—division of nuclei, hyperchromatosis, and possibly a granular change spreading from the poles of the nuclei.

Among the second series of changes those affecting the blood-vessels and interstitial tissue are found: (*a*) Cellular exudation around the blood capillaries (Fig. 3). (*b*) Exudation into and swelling of the interstitial tissues—which when extreme give rise to the appearance of an intramural nodule. (*c*) In the chronic cases perivascular fibrosis (Fig. 4) and the occurrence of new-formed strands of connective tissue running in the intermuscular septa, and replacing in part the muscular tissue (Fig. 5).

The papillary muscles of the mitral valve, upon which depends in great part the effective action of the valve, are often seriously damaged.

¹ Arch. de Méd. Expér., 1895.

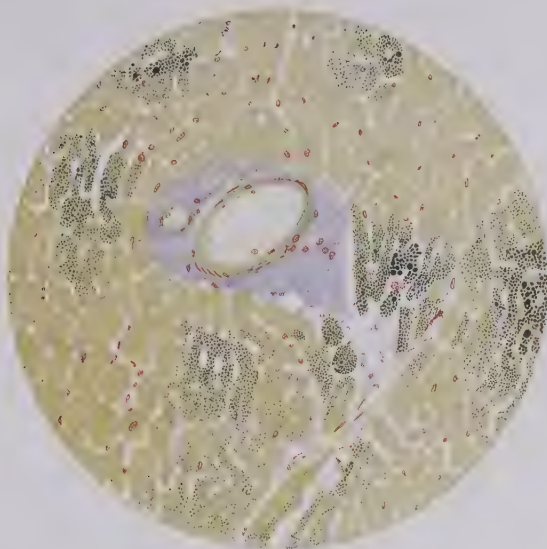


FIG. 2.—A section through the left ventricle of a case of rheumatic carditis to show fatty change in the muscular fibres in the neighborhood of a capillary blood-vessel.

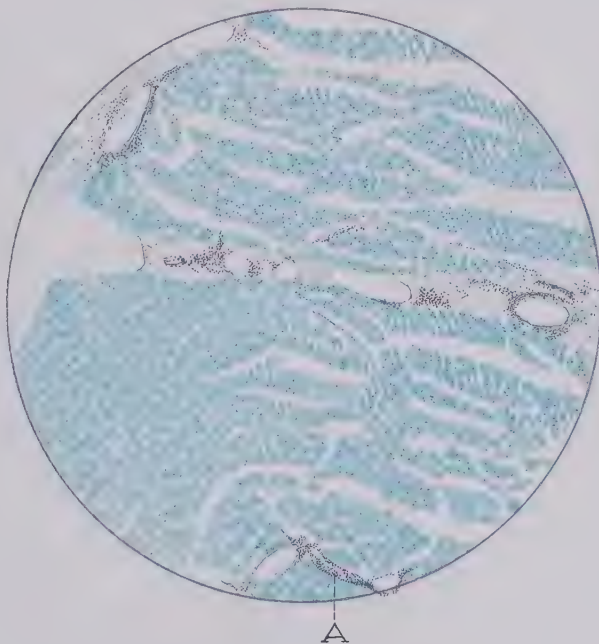


FIG. 3.—A section through the left ventricle of a case of rheumatic carditis to show cellular exudation in the interstitial tissues. A, cellular exudation.

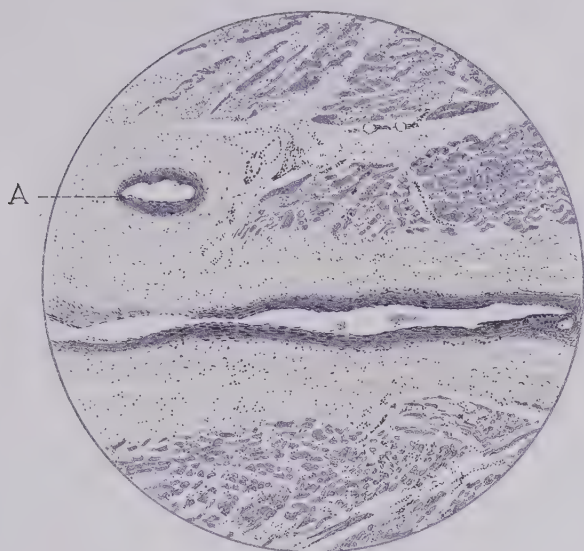


FIG. 4.—A section through the left ventricle of a case of chronic rheumatic carditis. A, a blood-vessel with much perivascular fibrosis.

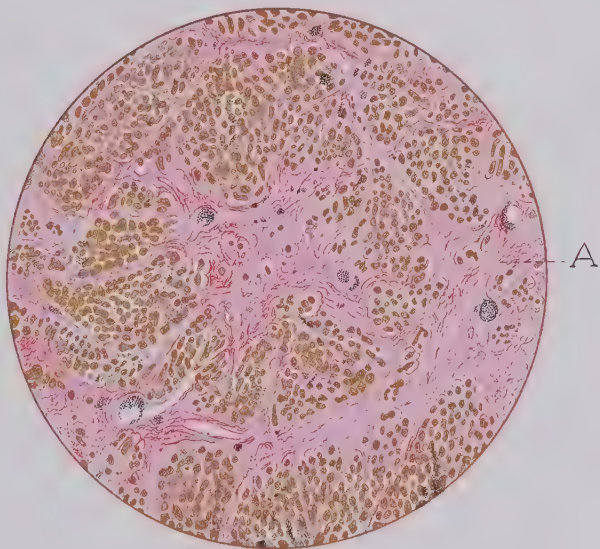


FIG. 5. A section through the left ventricle of a case of chronic rheumatic carditis showing interstitial fibrosis. A, the fibrous tissue.

I have arranged these pathological changes in the cardiac wall in this way for a special reason. I am anxious for you to rid yourself of the word myocarditis. Inflammation is only one process of disease, and that probably a reparative one dependent on the presence of blood-channels. In rheumatic fever, as in other infective diseases, there are at least two processes: (1) those the result of the toxins damaging, for example, the muscle, not by inflammation, but by a poisonous action, and (2) the inflammatory changes taking place in the regions of the minute blood-vessels.

In some cases the deleterious effects of the toxins are more marked than in others, and there are on the other hand, I am sure, some cases in which, after repeated attacks of rheumatic fever, the muscle remains sound. To speak, then, of rheumatic affections of the myocardium as a rheumatic myocarditis is to take too narrow a view of the question. Nor, for my part, have I any belief in the inflammatory changes spreading into the heart wall from the valve rings or pericardium. I think there is in rheumatic fever a blood infection of the entire heart through the coronary circulation, and if the heart wall suffers it is a direct result of this infection, as are endocarditis and pericarditis.

The drawings illustrate:

Fig. 2. The fatty changes in the muscle.

Fig. 3. The cellular exudation from a blood capillary.

Fig. 4. Interstitial cellular exudation and fibrosis.

Fig. 5. Perivascular fibrosis.

This macroscopic specimen, preserved by the Kaiserling method, shows what you may have seen yourselves in the post-mortem room—the pallor of the cardiac muscle in a case of severe rheumatic carditis. And this macroscopic specimen is a most striking example of rheumatic dilatation. The patient died in a first attack from progressive heart failure. There was no pericarditis, and though there was endocarditis of the mitral valve, there was also great myocardial damage.

It is most unfortunate that the right ventricle has been removed in order to get the specimen into the jar, for when I came to examine the wall of this ventricle, I found upon the outer surface two projections which I can only compare to the blister-like excrescences upon a Higginson's syringe which has been overstrained. At those two spots there was practically no muscle at all, only the visceral

pericardium intervened between the blood in the right ventricle and the pericardial cavity.

Imagine what might have happened if this dilatation had been mistaken for pericardial effusion and paracentesis attempted!

I fear these details have been somewhat wearisome, but they have enabled me now to approach the clinical side of the subject with the confidence of a basis of some assured fact, and I will now turn to some of the important clinical bearings.

II

The first point of clinical importance is this: the earliest evidence of rheumatic heart disease may be a dilatation.

I do not mean for one moment to say that other infective diseases do not cause dilatation, for we know that they do: instance only diphtheria and influenza, upon which an important paper was written by Dr. Lees.¹ But it is very important to remember that dilatation may be the first evidence of rheumatic heart disease.

The earliest physical signs of this dilatation I gave in my first lecture, but let me repeat them again here. They are: (1) An increase in frequency and a lowering of the tension of the pulse. (2) An outward movement and feebleness of the cardiac impulse. (3) An increase of the deep cardiac dulness to the right and left. (4) A shortening of the first sound over the impulse and an accentuation of the second sound at the pulmonary base. (5) In some cases a soft systolic murmur heard most clearly internal to the nipple.

Now, amidst all the uncertainty that there is about the treatment of rheumatic heart disease, it really does seem clear that rest is of great value, and may (who can say does?) cut short a severe attack. The earlier rest can be obtained the better I think is the outlook, and so the detection of early dilatation is a practical and valuable achievement.

The second clinical fact of cardinal importance is this: The great enlargement of the cardiac dulness which may occur in acute rheumatic pericarditis is more often the result of dilatation than of a large pericardial effusion.

You will at once see the importance of this as a guide in treatment. If this great enlargement of the cardiac area was usually

¹ British Medical Journal, January 5, 1901.

the result of effusion, we should be led to the conclusion that this effusion must gravely embarrass the heart, and be an imminent cause of danger. Further, we might hope to relieve the heart by a timely paracentesis. But if it is a dilated and feeble heart which is the main cause of the cardiac enlargement, not only should we be disinclined to introduce a needle, but we should actually fear to do so, lest, piercing the diseased ventricle, we precipitate death.

To make this the more clear, I will give you first the impression I gained of acute pericarditis from my education when a student. I learnt that there were three phases: (1) The early stage of cardiac excitement and early pericardial friction; (2) the second stage of pericardial effusion; and (3) the third stage of resolution and late pericardial friction. The second stage, that of effusion, was characterized by an enlargement of the cardiac area, muffling of the heart sounds, and a tumultuous action of the heart. If the effusion was very great, the fluid would need to be drawn off.

Now, there is no doubt that a great enlargement of the cardiac area in rheumatic pericarditis is a very frequent occurrence, and I have seen enormous enlargements more than once. The inference would be, then, that a great effusion was frequent in rheumatic heart disease.

But when, in 1898, I examined our post-mortem records and collected 150 fatal cases of rheumatic heart disease, I found that in only 35 had the amount of fluid in the pericardium even attracted especial attention, and in only 12 of these cases had more than 2 ounces been measured, and in only 6 cases, more than 3 ounces. The explanation is clear. The great enlargement of the cardiac dulness in rheumatic pericarditis is, as a rule, due, as Sir William Gull taught, to dilatation of the heart, rather than to effusion. If you wish for more evidence still, it may be added that investigators have introduced needles through the chest wall after death, and have found that instead of passing them into a distended pericardial sac, they have passed them into the cavity of the heart itself, and on more than one occasion during life, blood has been drawn off instead of exudation, and even a fatal event has resulted from such a procedure.

The lesson, then, that is learnt is a very real one. Picture yourselves face to face with a severe rheumatic pericarditis. The child is breathless, distressed, and, you fear, going to the bad. You are

harassed by conflicting thoughts; you know that a large effusion oppresses the laboring heart, and you know that rheumatic pericarditis is not, as a rule, fatal. You feel that if you draw off the fluid you may bring relief, but that if you fail or pierce the heart you may turn the scale against the child. What an aid it is—and I can speak from experience—to realize that an effusion sufficient to oppress the heart is rare in rheumatic pericarditis, but that dilatation is very common. For now it is clear that unless you have the most certain indications of a large exudation, you do not interfere.

I think it is my duty to attempt to give you some points in the differential diagnosis between a dilated heart and pericarditis with effusion, for it may happen to any one of us to be confronted with an exceptional case in which there may be very great difficulty in settling this point.

In the first place, we are much helped by a knowledge of the course of the disease. The doctor in every-day attendance is in a better position to judge than the consultant who sees the case once. For when a large effusion follows on pericarditis, you may trace the heart sounds becoming more faint and muffled day by day, and only the attendant who pays frequent visits can truly realize this sign. It is a very important one, for in rheumatic dilatation the sounds, though they may be feeble, are usually clear and distinct. I must admit that there are cases in which the heart is bound to the front of the chest by adhesions, and in which fluid collecting in the pericardial sac behind pushes it forward, but these exceptional cases do not alter (to any appreciable extent) the value of the point I have already mentioned.

The pulse, in a case with large effusion, may be small, rapid, and very irregular; in dilatation, though the tension is low and the pulse rapid, it is not such a small and irregular pulse, for the movements of the heart are not embarrassed as they are by a large effusion.

Disappearance of the impulse is in favor of a large exudation, a diffuse impulse in favor of a considerable dilatation. You are more likely to feel the impulse in dilatation than in pericardial effusion. As for dulness in the fifth right interspace (Rotch's sign)—I have been disappointed with this sign in rheumatic pericarditis, and I am convinced that a dilated right auricle will give the same sign in those very cases in which you are likely to be in doubt.

A toneless dulness in sharp contrast to the pulmonary resonance, and a dulness which gives a marked sense of resistance to the fingers, point to fluid.

The angle which the right lower margin of the cardiac dulness makes with the hepatic dulness is perhaps more useful. Dr. Ewart has especially insisted upon it. But it is a refinement which requires exceptional skill and accuracy. Further, it is not always reliable, as I have proved for myself in the post-mortem room. This angle, formed by the right margin of the cardiac dulness meeting the horizontal hepatic dulness, should be acute in dilatation because of the curve of the auricle, but obtuse in a large effusion, because the pericardial sac becomes distended. This is made quite clear by these simple diagrams (Figs. 6 and 7).

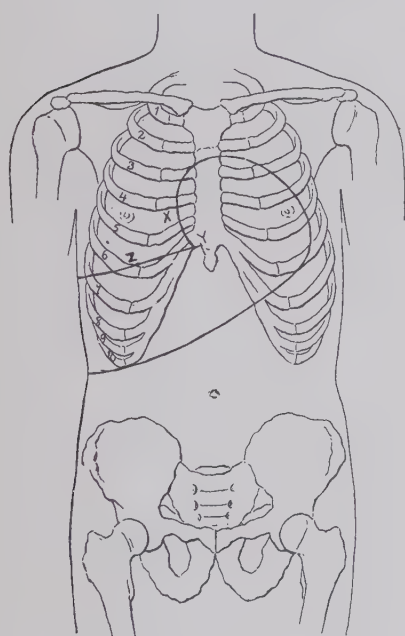


FIG. 6.—Z, the line of the hepatic dulness; X, the curved line of the right auricle; X Y Z, the acute angle formed by their junction.

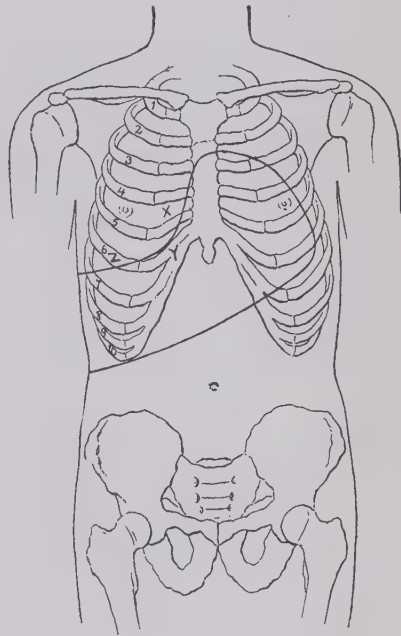


FIG. 7.—Z, the line of the hepatic dulness; X, the line of the distended pericardium; X Y Z, the obtuse angle formed by their junction.

The third and last clinical point I shall deal with is the one which I wish to illustrate to you to-day by clinical cases, and I will introduce it to your notice in the form of an interrogation.

Is it not possible that in rheumatic fever the cardiac wall may

be damaged out of proportion to the cardiac valves or pericardium? The answer, I feel sure, is yes.

There are two clinical types,—the acute and fatal cases, which are very rare, and the chronic cases, which I think are much more common, and of which I show you four examples.

The acute cases I must, for lack of time, dismiss in a few words. They are cases of rheumatic fever which die rapidly of cardiac failure, and in which after death no pericarditis is found, and perhaps no endocarditis or only the very slightest and earliest.

But the condition I am especially interested in now is a more or less persistent cardiac weakness following a well-defined or vague attack of rheumatic fever. There has not been any pericarditis and perhaps no endocarditis, but the heart remains weak and large, the patient breathless and nervous, and recovery is evidently imperfect.

They form an important group of cases, not only in the diseases of childhood, but, because of their bearing upon the etiology of obscure cases of dilatation of the heart, in adult life.

CASE I.—This boy first came under observation in September, 1900, and was then 10 years of age. Four weeks before being seen he had got wet through twice in one day, and shortly afterward developed a sore throat and pains in the head, followed by pains in the chest and abdomen. The house in which he lived was damp, but he is very well looked after by his mother. When I saw him he looked ill, there was arthritis of the knees and hips, and a rapidly acting heart with a systolic mitral murmur. The temperature was raised to 100° F. The boy was admitted to the hospital, and when I saw him again in October a mitral murmur was still present.

It was not until May, 1902, that I saw him again, and during those 18 months he had kept well; but a fortnight before this second visit he had developed a sore throat and pains in the limbs. I found on examination no murmur; only a dilated, rapidly acting heart.

Since May, 1902, he has been again an in-patient, and I have never lost sight of him for any length of time, but have closely followed his case.

What is his condition now? Briefly this: he has an enlarged heart and the impulse is diffuse and well outside the left nipple line.

There has been no murmur, and no thrill or other evidence of a contracted or incompetent mitral orifice. There is no aortic disease, and there has never been to my knowledge an attack of pericarditis. The pulse-rate is always above 100. He cannot run, he is breathless on any sudden exertion, and with exertion there is pain over the heart. He is highly nervous and easily becomes "fagged" and anemic.

During the last few months there has been some improvement, and you do not see him now at his worst. I consider that in his case the myocardium is damaged, and that it is the heart wall and not the valves or pericardium which are in fault.

He is well worth careful examination, for you might easily underrate the gravity of the condition, because there are only the symptoms and the enlarged heart to guide you.

CASE II.—This case is of exceptional interest, and well illustrates the difficulty there is in separating the nervous and the muscular factors in any study of the heart wall.

I first saw this child in March, 1902, when she was suffering from a definite but not very severe first attack of chorea. She lived in a damp house close to the Thames, and her father had suffered from rheumatism. The feature of her case was tachycardia, and although she was taken into the hospital at once, the pulse-rate varied between 140 and 200 from March until the end of May. Long after the chorea had disappeared this tachycardia continued, but there was no swelling of the thyroid or protrusion of the eyes. During the illness the heart became dilated, and the condition was for many weeks very grave.

By September there was much improvement; later when I saw her, the pulse had fallen to 78, but, nevertheless, the heart was large and the impulse heaving. There was no cardiac bruit, and except for a short time while in the hospital there had never been the suspicion of a murmur, but there was dilatation of the heart, and later there was hypertrophy.

This child is very excitable, is easily rendered breathless, and although very much better the heart is not yet really strong.

It may well be that the poisons in this case acted more upon the nerve than upon the muscle, but the point I want to make is this: the heart wall suffered rather than the valves or the pericardium.

Here, again, we have a large heart, without a murmur. A highly nervous child, easily terrified, easily tired, short of breath, and apt to become anemic. Her breath is short, and the heart very irritable. I mean irritable in this sense, that on very slight provocation it beats rapidly and often irregularly.

CASE III.—This case is a more recent one. She is a little girl, aged 10, who had an attack of rheumatic fever at 3 years of age, and off and on since. The grandmother and grandaunts on the mother's side had suffered from rheumatism. In January, 1903, she was operated upon for adenoids, and about a week afterward a fresh attack of rheumatism commenced with a stiff neck.

She is a nervous, excitable child, always short of breath. The pulse is rapid, and when I saw her first was 125 to the minute. The impulse is excited, the area enlarged, but there is no murmur, and there has not been one since I saw her first in January. She is anemic, and the pulse easily becomes excited and irregular. At one time I suspected albuminuria, but did not find any in the urine, although it is quite probable there may be albumin occasionally. She is improving.

CASE IV.—This boy, aged 9½ years, came to me in May, 1902, with a history of not having been in good health for some time. He had suffered with headache, pains in the abdomen and limbs, and sore throat. He was also very nervous and irritable. When I saw him his heart was acting at the rate of 132 per minute and there was a diffuse impulse. The temperature was 99° F.

His mother preferred to keep him at home rather than leave him in the hospital. He improved under treatment, and I lost sight of him until September. He then returned with more pain and an excited heart. This time he was taken as an in-patient, the temperature being 100° F. and the pulse-rate 160. With these there were slight chorea and a diffuse impulse.

The heart was enlarged, the action rapid and excited, but there was no murmur, and there has not been one to my knowledge. I have never lost sight of him for any length of time, and have not any reasons for believing he has suffered from pericarditis, for he comes here whenever he is threatened with rheumatic fever.

This boy is slowly improving, and lately he has made decided progress, but the impulse is still diffuse and the cardiac area larger

than normal. He, just as the other children, is very excitable, easily tired, out of breath, and soon becomes anemic.

I have had other instances of this condition, but to multiply the cases might be only to obscure the point which I wish to make clear,—namely, that these children have weak hearts, not from pericarditis or endocarditis, but from some damage to the cardiac wall.

You may think that this interpretation of these cases is fanciful, but I have given you strong reasons for its acceptance, and further let me add that to my personal knowledge, such cases, both acute and chronic, have proved fatal, and post-mortem examination has shown the reality of the condition. Only last autumn Dr. Theodore Fisher showed me an example of the acute condition. And more recently Dr. John Broadbent showed me the damaged muscle fibers from one of these chronic cases, which had proved fatal with much dilatation at the age of 17 years.

What is the prognosis in this group of cases? To be frank I cannot tell you. I am not aware that they are very generally recognized, and I have not traced their histories myself for a sufficiently long time. I look upon them as grave cases, for they are very slow to improve, and easily upset by slight illness. I suspect that they will always be liable to palpitation and breathlessness on sudden exertion, but, provided they have no more attacks of rheumatic fever, I do not see why they should lose ground, and should not, on the other hand, slowly improve, as these have done.

Should cases such as these later in life take to alcoholic excess, I think they will appear in the ward of some general hospital as breathless, edematous patients, with large dilated hearts which refuse to react to treatment.

I mention this because I think the temptation to take alcohol is very strong in this class of patients. They cannot get through their work with comfort, and are easily depressed, because of their feeble hearts. How tempting to fly to stimulants! How incautious oftentimes are we also with such people! I feel sure that when you see these highly nervous children, you must realize how, through no fault of their own, in later life they are easily influenced and may take to the use of stimulants. Yet nothing could be worse for them than alcoholic abuse.

Finally, a few words upon their treatment. Whenever after rheumatic fever the heart remains feeble and rapid, rest is all

important. Glance once more at those drawings, and you will understand that the reparative changes *must* take time. When complete rest is abandoned advance cautiously. Graduated exercises, saline baths, and slow, steady, voluntary exercise, first on the flat, then up a gentle incline, now have their place. Many cannot afford these refinements. You can help them almost as much by curtailing and arranging their exercise.

A mother will bring her child and say to you: His spirit is stronger than his body. There is no better definition of a rheumatic child that I know, than this. Let us accept the accuracy of the definition and take the hint. Make these excitable children rest for one hour in the forenoon. The discipline itself is good for them, and if they are thin it is especially useful. I like to see rheumatic children get fat.

A practical difficulty in dealing with such cases is to discern how much of the cardiac excitement is due to nervous influences, how much to organic damage. The symptoms and physical signs must all be taken into consideration, and you must not be guided only by the pulse.

Drugs are of undoubted value, and our study of the pathology gives a clear notion of their rightful place. The best cardiac tonics will be those drugs which improve the general health and thus assist the reparative processes. In other words, you treat the child, he will treat his heart. Tonic doses of quinin in an alkaline preparation, cod-liver oil and malt, or a course of arsenic for some weeks at a time, carefully guarded by alkalies, as recommended by Dr. W. B. Cheadle, have helped me in the stage of convalescence. I do not like iron for rheumatic children, except in the most gentle preparations of the drug. The digestion is easily upset by iron, and then it does more harm than good. Bromids are valuable when tachycardia is largely the result of nervous excitement, rather than evidence of severe organic disease of the cardiac muscle.

Direct cardiac tonics such as digitalis and strophanthus are, as a rule, disappointing, and though I admit this to be a matter of opinion, I do not like the use of salicylates in large doses in these cases. The digestion and the bowels of these children require constant supervision.

I am often asked about the question of eating meats. I should like to divorce myself entirely from the "uric acid" enthusiasts, for,

in my opinion, they have gone far beyond facts and sometimes beyond reason. I maintain in opposition to them that there is no proof that meat does harm to the rheumatic child when he is convalescent, or in a state of rheumatic cachexia. On the contrary, I think it does good, and I always advise it in quantities suitable for a child of the particular age, with, I consider, good results.

Lastly, the rest treatment may be overdone. Children, I believe, suffer from this over-treatment. You see or hear of them feeling their own pulses! exaggerating every pain or throb! We must avoid this if we possibly can, and by using all our judgment try to bring about a happy result.

Surgery

COCAIN ANESTHESIA WITH ILLUSTRATIVE CASE— OPERATION FOR VARICOCELE

A CLINICAL LECTURE DELIVERED AT THE NEW YORK POLYCLINIC HOSPITAL AND
SCHOOL FOR GRADUATES IN MEDICINE

BY J. A. BODINE, M.D.

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GENTLEMEN: Our first patient this morning is suffering from a rather large varicocele. He comes to us to have it operated upon, because he is an applicant for a position in the New York City fire department, and the authorities refuse to take individuals suffering from varicocele of any considerable extent. The same thing, of course, is true in the police department and also in the United States army. The desire to enter any of these municipal or government services is usually one of the main indications for operation upon varicocele.

As a rule, varicocele should remain unoperated upon. The indications for operation are, (1) progressive atrophy of the testicle, especially if this induces sexual neurasthenia that makes the patient's life uncomfortable; (2) continuous lumbar pain that is a source of great discomfort to the patient and makes it difficult for him to perform his usual avocation, whatever that may be; and (3) a state of mental fixity with regard to the existence of this condition which prevents the patient from getting his attention concentrated on any other subject, and so makes his life miserable and useless.

This state of mental hebetude which comes on in cases of varicocele in young men is rather difficult to explain. It is very probable that the scarehead advertising literature in the daily papers with regard to this subject has a good deal to do with concentrating the mind upon it. Commonly these patients are not suffering from a severe form of varicocele, and it is extremely difficult to understand why they should have all the symptoms they claim to suffer from. These symptoms usually exist in neurotic individuals, and commonly

a distinct family heredity of nervous tendencies will be found. They constitute, however, a class of cases that is most obstinate to treatment and that becomes almost the bane of a doctor's existence, the patients are so annoyingly persistent in the explanation of their symptoms.

We are going to do the usual operation for varicocele in this case, but shall perform it under local anesthesia. No operation for varicocele justifies the employment of general anesthesia. The surgeon who uses a general anesthetic for the ordinary varicocele operation knows nothing of the possibilities of cocain anesthesia. It is true that this is a delicate sensitive region, but this constitutes no absolute contraindication to the use of local anesthesia. As you will see in the present case, the operation can be performed without giving the patient the slightest twinge of pain beyond the first prick of the hypodermic needle that begins the injection of the local anesthetic.

In order to accomplish this purpose properly a special technic is necessary. It is not enough to inject the cocain solution, but the operator must be himself thoroughly in touch with the patient's personality and have secured his complete confidence before success can be assured. There must be no flurry and no question in the patient's mind of the possible occurrence of pain. A single twinge of pain at the beginning of the operation, contrary to the patient's expectation, would make it impossible, for even a 10 per cent. solution of cocain, to produce perfect anesthesia.

Once the patient's confidence is completely gained, even the most serious operations can be performed under cocain. The abdomen may be opened and manipulations of the intestines accomplished. This has been done in a number of reported cases, and I have done it myself when it was deemed necessary for good reasons to protect the patient from the effect of a general anesthetic. Amputations may easily be accomplished under cocain anesthesia if there is any contraindication to the use of the general anesthetic. With less than a grain of cocain in a patient whose confidence has been gained, you may amputate the leg between the knee and the hip without a single complaint or a trace of nervous shock.

In order to succeed in cocain anesthesia there are three or four directions that must be given with regard to the cocain solution employed. First, it is a fundamental principle that the cocain solution

to be used for local anesthesia by hypodermic injections must never be more than 48 hours old. Stock solution may be used in the nose or throat, but should not be used under the skin. Even in the nose and throat old solutions will be found distinctly lacking in the anesthetic powers of the fresh solution. When recently dissolved, cocain solution is absolutely neutral. The salt is a neutral salt. In 48 hours, however, a cocain solution will be found to have become acid. Just in proportion to the extent of its acidity will it be found to have lost its anesthetic property. This is one of the reasons why, even in the nose and throat, when old solutions of cocain are employed, a solution of sodium bicarbonate is used beforehand in order to neutralize the acidity of the cocain solution and so restore its anesthetic property. If the nasal secretions are known to be acid, thorough douching must precede the cocain application.

In order to have a fresh solution, the cocain should be kept in tablet form and dissolved whenever needed. If tablets containing a grain are used, a solution containing a grain to the dram may be readily prepared. Here in the hospital, for purpose of convenience, we employ a stock solution of the strength of one grain to the dram, and to each dram of the solution we add a dram of an alkaline liquid made by dissolving a teaspoonful of ordinary bicarbonate of sodium in a pint of water. This slightly alkaline liquid is sufficient to overcome the acidity that develops in the cocain solution on standing and restores its anesthetic properties.

The second important consideration with regard to local anesthesia is that the local anesthetic should be warm when injected. A cold solution not only proves a source of irritation to sensitive nerve-endings when introduced under the skin, but it fails to have as much anesthetic power as a warmer solution. The liquid used should be of about blood heat. If it is less than 60° F. in temperature, its anesthetic effect is distinctly diminished. This is an important practical point for local anesthesia in office practice where the doctor is sometimes tempted to use solutions made with water of ordinary temperature. This is a common source of failure in perfect local anesthesia, especially in the winter time.

The third precaution with regard to the cocain solution is, that for successful local anesthesia the solution must be weak. With a cocain solution of about 1 per cent. in strength, or less, more perfect local anesthesia can be obtained than is possible with a 4

per cent. solution. Successful obtunding of sensibility requires the diffusion of the anesthetic through the tissues in such a way as to affect a number of nerve-endings. If the cocain solution is strong, this cannot be done without having sufficient absorption of the drug into the general system to produce symptoms of cocain poisoning. Two or more grains of a strong solution of cocain may be used for a small operation without producing the requisite insensibility of tissue, while with less than half a grain the leg may be amputated between the knee and the hip without causing the patient any discomfort.

A fourth practical point with regard to the use of cocain is that the antidote for cocain poisoning is morphin. It is not only a symptomatic antidote, but seems to be a physiologic neutralizer of the effect of cocain on the system. With the use of dilute solutions, symptoms of cocain poisoning need not be expected. But mistakes may occur, and then it is well to have a solution of morphin handy for use. By accident, here in the Polyclinic some time ago, the patient, who was himself a physician, was given an injection of a 10 per cent. solution of cocain instead of a 1 per cent. solution. His breathing became shallow and rapid, his pulse increased in rapidity, he became aphasic, and tremor of all his muscles set in. He was utterly unable to stand, and had lost the power of muscular movement. A quarter of a grain of morphin was given, and in ten minutes his symptoms began to abate, and in fifteen minutes he was practically recovered.

Schleich, the German surgeon who introduced what he called infiltration anesthesia, some ten years ago, used a certain amount of morphin in the solution which he recommended. The cocain was dissolved in salt solution and a small quantity of morphin added. There is no necessity for this, however, and it is better to withhold the use of the morphin until it may be needed. Occasionally when patients are of an extremely nervous disposition, and are suffering from intense emotion before an operation that is to be done under local anesthesia, it may be advisable to give a small amount of morphin some twenty minutes before the operation is performed. To the great majority of people two-thirds of a grain of cocain may be given without inducing the slightest symptoms of cocain intoxication.

It is important to remember that while morphin is the direct

antidote for cocain, cocain is also the best antidote for morphin. Not very long ago, at one of the hotels in New York City, a guest who had taken an overdose of morphin seemed to be moribund. He was comatose; his respirations were so shallow and infrequent, not more than two or three to the minute, that his blood was almost entirely unoxidized, and he was so cyanotic as to be quite black in the face. The case seemed utterly hopeless. He was given a quarter of a grain of cocain, and his symptoms began to improve almost at once. At the end of fifteen minutes his respirations were seven or eight to the minute, and he was given another quarter-grain of cocain. His symptoms continued to improve until the morphin poisoning was practically entirely overcome. Unfortunately, however, he died some twelve hours later from edema of the lungs.

It is important that the patient should not be surprised by anything that is done. Warning should therefore be given of what is about to be done, and some explanation of what his sensations will be should be told him. We begin the local anesthesia in this case not near the root of the penis, where there are a great many sensitive terminal nerve-endings, but lower down in the scrotum, which is comparatively insensitive. The first prick of the needle is made into absolutely normal tissues, and is bound to produce the slight pain incident to the penetration of the point. We frankly tell our patients this, and then proceed to insert the needle.

This form of anesthesia is said to be done by hypodermic injection. It is to be remembered, however, that we do not insert the needle through the skin, but rather into the skin. It is really endodermic injection. If you will notice here, the point of the needle is inserted barely underneath the epidermis. Only a very small drop of the fluid is forced out of the syringe, because the presence of any considerable amount of liquid would by its pressure produce pain. When the needle is withdrawn, care must be taken to reinsert it within the anesthetic area produced by the first injection. We thus continue our work always through preanesthetized tissues.

It must be borne in mind that the patient is all this time in the state of extreme nerve tension. He should be questioned occasionally if perchance he is feeling any discomfort, for it is possible that some mistake in the technic may slip in that will only be recognized by having the patient tell of the pain he feels. The patient's confidence must always be retained, and even occasionally he should be

assured that if he feels any pain the operation will be continued, should he desire it, under general anesthesia.

It is always important not to make the punctures of the needle at random, here and there and everywhere, as you sometimes see surgeons do, but to proceed carefully, following up one puncture with another in the immediate neighborhood, until the skin is thoroughly anesthetized. A needle prick is not a very serious torment, and yet a series of them in the midst of the nervous strain that the patient is already under, is sufficient to produce an almost incalculable amount of torture. In old times it is said that they sometimes ingeniously tortured criminals by allowing drops of water to fall at intervals on their heads. After a while this monotonous dropping proved a source of almost unbearable torture, and prisoners became insane because of it. The methods of procedure of some surgeons would remind one of this old-time diabolical torment.

After the skin has been thoroughly anesthetized a solution of cocain somewhat weaker in strength may be used for the deeper tissues. In producing the skin anesthesia we used a solution of cocain one grain to the dram diluted to one-half strength by the bicarbonate of sodium solution already described. For the deeper tissues we shall now use a still more dilute solution containing about an eighth of a grain of cocain to the dram.

After you have completed the production of the local anesthesia do not turn at once and ask for a knife. That is of itself quite enough seriously to disturb the patient's equanimity, and will make him jump as soon as the pressure of the steel is felt on him. This precaution is especially necessary when patients are women. Either nod to your assistant, who should understand what you mean, or ask for a bistoury, a term usually not understood by ordinary patients. In the present case we shall not employ a knife, but a scissors, which somehow does not convey as much dread to the patient's mind.

Remember to be careful in swabbing out wounds made under local anesthetics. Rough swabbing may easily cause much more pain than a clean cut. Do not rub across the tissues with a piece of gauze. The field of operation may be kept free of blood by gentle pressure with a gauze sponge. It must be remembered that all vessels have vasomotor nerves in their coats and that a vasomotor nerve possesses a certain amount of sensibility. The vessel cannot be cut without producing a certain amount of pain, and,

as a rule, the cocain injected does not succeed in finding its way to the principal nerve-endings of the vasomotor nerves. The pain of cutting an artery is only slight, but the patient should be warned that he is going to feel it, for this lessens his discomfort by removing the surprise. Unexpected pain is what must be avoided. If an artery has to be caught with an artery forceps, or tied, even more pain will be inflicted than in merely cutting the artery. The patient should be warned of this also. The discomfort caused is, however, not very serious and lasts but for a moment.

We have now completely exposed the spermatic cord. We can handle it without producing any sensation of pain. We now assure the patient that the operation is nearly over, for by thus keeping him informed of the progress of the operative work we lessen the nervous tension and the strain of expectation. The cord should be handled somewhat carefully, and especially the vas deferens must not be pinched between the fingers, as this causes pain.

It is not difficult to discover the vas deferens and to locate it exactly. As the veins are rolled under the finger they collapse. The vas deferens, however, remains as a rounded cord not unlike a leather shoestring. The amount of pressure necessary to discover this is not sufficient to cause the patient any discomfort.

We have now separated the veins from the vas deferens, and we proceed to put a ligature around them. Our first ligature is tied at the highest point, because by so doing we shut off the nerve-supply from the lower part of the cord. As vasomotor nerves occur not only in arteries but in veins also, we can be sure than in tying this ligature we will produce some pain. If we tied it below first we would cause this pain twice, instead of once. But now, when we come to tie the second ligature lower down, the nerves to the vessels will have been deadened by the first ligature. Besides, we shall be able to empty the veins of the blood that collects in them below the first ligature, and so prevent the production of a certain amount of venous congestion by our ligature.

Our patient says that his hands are numb, and he seems to be a little bit afraid lest we should have given him so much cocain as to cause this numbness. You notice the position he has been lying in, with his hands under his head. It is the position a man will often assume when he is about to have an operation done under local anesthetic. For a time the position is comfortable, but then

there comes interference with the circulation in the arms, and the fingers are apt to get numb. This is what has happened here, and I tell him simply to put his hands down alongside his body and they will recover their feeling almost at once.

We never curtail the scrotum in these operations here, and I think it always a mistake ever to suggest the removal of a flap of scrotal tissue. The muscular coat of the scrotum, the dartos, is very retractive, and will bring back the scrotum to its normal size as soon as the weight of the enlarged veins is removed from it. This will occur even if the scrotum should be distended half-way to the knee. In order to allow for immediate scrotal retraction, however, we remove the weight of the testicle completely from it, and in order to do this we tie the ends of the ligatured veins together, the ligatures having been purposely left long for that reason.

Sometimes as the result of the relaxation of the intense nervous strain to which patients are subjected, during an operation under local anesthesia, they may vomit after the operation. This will usually occur only in neurotic people. You can look for it sometimes in women, however, and should usually warn patients not to have too much food on their stomachs when they come for operations. An important personal matter for the doctor is to have patients deliberately settle for themselves before they leave the table what were their feelings during the operation. The memory of the nervous tension through which they went is apt to come back to them as a feeling of torment. As the result of this false memory they are prone to an exaggeration of the physical pain they suffered. Such patients, when asked about their operations later on, are liable to say that while there was no severe pain, the operation was a dread ordeal. It is well, then, to have them fix their feelings definitely by asking the question, "Now, did you feel any pain?" The prompt reply is, "No." Patients when thus questioned are not apt to discourage other patients from having operations done under local anesthesia, while if left to themselves a false memory might make them do so.

Personally I am of the opinion that local anesthesia has a much wider field of usefulness than is at present conceded to it. I have now had experience of its use in 33 operations for hernia, 7 of the patients having been medical men, and I think it only proper to say that the employment of a general anesthetic seems almost un-

justifiable in the performance of a radical operation for an ordinary uncomplicated hernia. It is often said that while patients do not suffer severe pain during surgical measures with local anesthesia, they do suffer from an intense nervous strain that makes the whole time of the operation a hideous nightmare, which they would not care to go through again for worlds. In the cases of my medical patients I have asked for and obtained certificates from each of them, declaring not only that they suffered no pain, but that the nervous strain during the operation was not severe.

Of course, it is important for this purpose that patients should have supreme confidence in the operator and should be well under the influence of his personality before the operation is undertaken. If patients are very nervous, or if they are aroused to extreme sensitiveness by some accidental infliction of pain because of a faulty technic, then it will be impossible to do an entirely painless operation under local anesthesia. When confidence exists, however, and when proper precautions are taken, there is no reason why many operations that are now done under general anesthesia, should not be accomplished under local anesthesia.

GENERAL ANESTHESIA

THE ORATION IN SURGERY DELIVERED BEFORE THE KENTUCKY STATE MEDICAL
ASSOCIATION, AT LOUISVILLE, 1903

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THE subject which I have chosen for your consideration, "General Anesthesia," in my humble opinion, is second in importance to none in the domain of surgery. In dealing with it, while I cannot hope to furnish you anything new or original, I shall endeavor to present the subject-matter in such a plain and practical way that I may hope to be helpful, at least, to the busy general practitioner of medicine and surgery.

Experience of thirty-five years in the practice of my profession in a small town, and surrounding country, affording me frequent opportunities for the personal administration of an anesthetic, or the entire responsibility and oversight of it, has determined me to speak of that which I myself have seen and verified, rather than that of which I have only a theoretical knowledge.

I feel amply justified in dealing with the practical rather than with the theoretical or scientific aspect of my subject, in view of the fact that it is the general practitioner who, in squalid tenement, in remote country, without hospital or skilled assistant, at "mid-night's holy hour, when silence broods over a still and pulseless world," very frequently having himself first induced the anesthesia, must intrust it to unskilled hands, and then reduce dislocations, adjust fractures, return hernias, use the trephine, amputate limbs, apply the forceps, and even perform laparotomies.

To the honor of our country and to the everlasting credit of the medical profession of America, "General Anesthesia" was first demonstrated in the Massachusetts General Hospital, in May, 1846. Upon that occasion, when Dr. Warren performed the first operation under ether administered by Morton, he little realized that he stood upon the threshold of the most important era in the annals of surgery. The door was then opened and the path made clear

for the colossal achievements which have steadily marked surgical progress from that date until the present hour. The discovery and demonstration of the use of chloroform as an anesthetic by Sir James Y. Simpson, of Edinburgh, Scotland, in 1847, one year later than Morton's discovery, was the next most important step in the history of anesthesia. This discovery brought lustre to the name of Simpson and fadeless honor to the land of the sturdy Scotchman. So complete an innovation as was presented in the discovery of anesthesia, uprooting and revolutionizing existing methods, necessarily provoked severe criticism and opposition from the orthodoxy.

Most opportunely for the great discovery, its infancy coinciding with our war with Mexico, it was not long without an opportunity to demonstrate its claims for recognition. However, its complete christening came in the Crimea, in the gigantic struggle between Russia and the allied powers, in 1854-55. But it was left for our own great war between the States to give it its real baptism of blood, and send it on its triumphal march down the century, until to-day, wherever in the civilized world the art of surgery finds a votary, anesthesia sits enthroned at the head of the surgeon's table.

It is not only remarkable, but also creditable to the discoverers, that ether and chloroform, the two agents which were first used for the purpose of anesthesia, have never been displaced or superseded, but to-day head the list for safety and efficiency. Although nitrous oxid, ethyl bromid, methylene chlorid, anesthol, and other agents have been brought forward to contest for supremacy with the two older and better known anesthetics, yet it has never been demonstrated that any one of them is the equal or the superior of ether or chloroform.

Nitrous oxid, one of the oldest and safest of the anesthetic agents, until recently so much in use by the dentists, is now frequently administered in conjunction with ether. The nitrous oxid is used to tide the patient over the first stage of ether narcosis which is so trying and disagreeable. After the patient has passed into the stage of insensibility the ether is substituted, and the anesthesia is completed with that agent. The method of giving nitrous oxid with the free admixture of pure air or oxygen gas has done away with many of the disagreeable effects which formerly accompanied the administration of ether.

The administration of chloroform combined with nitrous oxid or with oxygen gas is much practised in the hospitals, and is said to lessen very materially the danger and the disagreeable effects connected with anesthesia by chloroform.

Mixed anesthetics, the A. C. E. mixture so popular in England, the Billroth mixture, and the Vienna mixture, all combinations of ether, alcohol, and chloroform in varying proportions, were very much used several years ago, and are still popular in some quarters. The effort in all these mixtures has been to combine the pleasant features of chloroform with the safe features of ether, to which are added the stimulating effects of alcohol.

It is strange that these mixtures have been lauded by many eminent surgeons, who declare them to be safer and more efficient than either ether or chloroform used separately; on the other hand, just as eminent men have denounced them as only mixed evils.

If the theory of Schleich is to be accepted,—that the amount of absorption of an anesthetic agent depends upon two factors, the body temperature, and the boiling-point of the agent,—then we will find no difficulty in reconciling the discrepancy between theory and actual experience as to the safety of these mixtures. If they are real chemical solutions and not mixtures, as is claimed by Schleich, having only a single rate of diffusion dependent on a new boiling-point different from any of the three components, it is plain why these mixtures really ought to be safer than either ether or chloroform used separately. The boiling-point of the A. C. E. mixture is 119° F., that of chloroform 149° F., and that of ether 93° F. In England 15,000 administrations of the A. C. E. mixture have been made without a death.

Any anesthetic whose boiling-point (the point of most rapid evaporation) closely corresponds with the body temperature, which in the lungs is 100° F., theoretically ought to be safe, for the reason that the anesthetic will not accumulate in the system, the lungs exhaling at each expiration as much of the agent as is taken in at each inspiration.

Dr. Meyer, of New York, presents to the profession, in a late paper on the "Improvements of General Anesthesia on the Basis of Schleich's Principles," a new anesthetic bearing the name of anesthol. It has been constructed on the principles laid down by Schleich, and Dr. Meyer, after an experience of four years, con-

siders it the safest, the most efficient, and the most pleasing anesthetic in use. Coming with such emphasis from such authority I can but commend it to your earnest consideration.

I must pass from the discussion of these agents, both new and old, to the consideration of ether and chloroform, the two agents which have borne the brunt and burden of the battle for general anesthesia for a half-century.

The essentials of any anesthetic must ever be: (1) its safety, (2) its efficiency, and (3) the ease and comfort with which it can be administered. No anesthetic, yet discovered, completely fulfils these requirements. Fatal results, while not nearly so frequent as formerly, now and then follow the administration of them all. Indeed, any agent which carries the patient so closely to the border line between life and death must be ever viewed with apprehension.

In many respects chloroform is the ideal anesthetic; it is rapid in action, pleasant to inhale, non-irritating to the air-passages, and less apt to be followed by nausea than ether. On the other hand, while ether is slower in its effect, less pleasant to inhale, more irritating to the air-passages, more liable to be followed by serious after-complications, and more apt to be followed by nausea, yet it is a certain and effectual anesthetic, and above all is five times as safe as chloroform. For this latter reason alone it deserves to stand at the head of the list.

In my judgment, if we only had an anesthetic agent which combined the pleasant features of chloroform with the safety of ether, we would have realized the ideal in this field.

Both ether and chloroform should always be found in the armamentarium of every surgeon, that he may be able to choose that agent which he may deem best suited to the case in hand.

Chloroform should be preferred in advanced renal troubles, in diseases of the air-passages, in surgical procedures about the head, face and mouth, nose and throat, in persons of advanced age, in children, and in parturient women.

Chloroform is peculiarly adapted to children. They take it well and with comparatively little danger. Most children, if carefully approached and their fears allayed, will take it without fright or struggle. But some of them must be held fast while the anesthetic is administered—in which cases danger may arise unless we are careful. In our effort to push the chloroform upon them rap-

idly, that the resistance may be quickly overcome, we are liable to overwhelm the patient. To avoid this danger, just so soon as the patient surrenders, we should remove the inhaler and allow free admission of air, until the respiration is natural, then cautiously push the anesthetic again.

Parturient women take chloroform more readily and more safely than any other class of patients. I believe, however, that it prolongs labor in many cases, and renders the patient more liable to hemorrhage after protracted administration. In operations connected with difficult labors when it has been necessary completely to anesthetize the patient, I have never seen a single instance in which serious danger seemed to threaten from the use of the anesthetic. Women in protracted labors are usually ready for an anesthetic, anxious to take it, take it without fear, and succumb to it quickly without resistance. In my opinion the brain of a parturient woman is in a state of congestion induced by contraction of the muscles of the neck, incident to the pains of labor, and this condition is antagonistic to the dangers which arise from chloroform anesthesia.

In these cases and in other emergencies, the physician after beginning the administration of the anesthetic is frequently compelled to intrust it to unskilled hands. The person to whom the anesthetic is intrusted should be instructed to maintain the anesthesia by keeping the cone about three inches from the face of the patient, and watching the respiration closely; if it becomes unnatural or noisy, he should remove the cone entirely until the breathing is quiet, then return the cone again to its former position. I prefer the cone to the inhaler in the hands of the unskilled, as they are sure to make a botch of the drop-by-drop method.

In reducing most fractures and dislocations, anesthesia is indispensable. I prefer chloroform to ether in these cases, especially if I am alone and have to use the anesthetic myself or intrust it to an unskilled assistant. The required anesthesia is usually of short duration; chloroform is more quickly and more easily administered, and muscular rigidity is more rapidly overcome. Dislocations which are nearly impossible of reduction without anesthesia, seem almost to reduce themselves under its relaxing influence.

In field surgery chloroform presents many advantages and is usually preferred. In organic disease of the heart it is not desirable

to use any anesthetic, but if one must be used ether should be selected.

Ether, without doubt, is the world's accepted anesthetic, and is by far the safest agent for general use and should be administered in all capital operations, in all cases of prolonged anesthesia, indeed, in every case in general practice requiring the use of an anesthetic, unless there is some good reason why it should not be used.

Whenever an anesthetic is to be administered everything in connection with the operation should be in absolute readiness, that there may not be a moment's loss of time. The dangers of anesthesia are materially increased by prolonged administration. The surgeon should never hurry, always taking time to do his work carefully and thoroughly; still there should be no loitering or unnecessary delay.

No patient except emergency cases should be subjected to an anesthetic without preliminary preparation. The diet should be regulated and restricted for several days previous to the day set for the operation; the alimentary canal should be thoroughly cleansed by purgatives in advance; no food should be allowed for six hours before beginning the anesthesia. The hour for the operation, when practicable, should be between six and ten o'clock in the morning; the stomach is then entirely free from all food and the patient's strength is at its best.

In emergency cases, one will frequently find the stomach filled with food, especially in children, who nearly always have one day's rations in their haversacks. In cases with full stomachs, retching and vomiting occur in the majority of instances soon after the anesthesia has begun. The safe as well as the wise thing to do is to stop the anesthetic at once, turn the patient on the side, lower the head, and allow the stomach thoroughly to empty itself before proceeding. If the stomach is empty retching and vomiting are indications for pushing the anesthetic.

When practicable the urine should be submitted to examination in every case, preceding the day for operation; the heart also should be examined preceding the operation, and should be re-examined by the person who administers the anesthetic just before he begins.

By whom ought an anesthetic to be administered? This is a most difficult question to answer, for circumstances alter cases. Certainly in hospitals, and when possible in private practice, the

administration of an anesthetic should be intrusted to one who has had both training and experience in this line of work. It is certainly a most responsible position, second in importance only to that of the operator himself. The question becomes vital when we consider that the consensus of opinion seems to be that the deaths from anesthesia are largely the result of faulty administration.

I believe the time is near at hand when professional anesthetizers will be found in every community who will be called in every case, when it is practicable, to administer the anesthetic and who will be expected to render a liberal bill for their services to the patient, just as the surgeons now render theirs.

Our medical colleges should send out no student who has not had special and practical training in the administration of anesthetics. It must, however, be remembered that no amount of training can make skilful anesthetizers out of some physicians. Some men have a peculiar adaptability for this work, which does not belong to and can never be acquired by others. The person who undertakes to administer an anesthetic should be a man of caution and of courage; he should be able to concentrate his mind completely upon the work before him; his eye must ever be on the watch, and his faculties on the alert. He must be wide awake; not an absent-minded day dreamer; he must be quick to note the danger-signals, and resourceful in meeting them.

The purity of the anesthetic must be beyond question. The patient who is about to take an anesthetic should be loosely and warmly clad. The operating-room should be quite warm, but not stifling, for two reasons,—the patient needs the pure fresh air, and the operator and his assistants are entitled to a reasonable chance for life while they are administering to the needs of a fellow-man.

All foreign substances should be removed from the mouth of the patient. Timid persons should be anesthetized before being brought into the operating-room. The patient should have the kindly assurance of the surgeon that he will take good care of him, that everything possible will be done to carry him safely through the operation, that the anesthetizer is competent and careful, that the anesthetic will be given slowly, that the operation will not be begun until he is thoroughly under its influence, and that he shall not be allowed to suffer during the entire time.

This is a far more important matter than you might imagine;

this is a new experience to the patient—he is not so familiar with these scenes as is the surgeon, and it should be remembered that the patient is not the surgeon, and that the surgeon is not the patient. A word from the surgeon spoken confidently and sympathetically will go a long way to quiet the fears of the sufferer.

In answer to the patient's question as to the danger of taking an anesthetic tell him, yes, there is some danger, but it is slight, just as he encounters every day of his life, in riding in a buggy, or upon a railroad train, or an electric car,—no more.

The face of the patient should be anointed with vaselin, especially if chloroform is to be used, to prevent blistering. Be careful, when the patient struggles or moves, not to drop the chloroform or ether into the eyes; this has been done, and may give rise to serious inflammation.

In hospitals there should always be at hand ready for immediate use, digitalin, strychnin, nitroglycerin, nitrite of amyl, tongue-forceps, mouth-gag, oxygen gas, and an electric battery. The two latter cannot be conveniently carried by the surgeon in his general practice. For the administration of chloroform, the Es-march inhaler is all that can be desired; it is simple, cleanly, and admits air freely—the prime requisite. For ether inhalation, the old-fashioned cone or Allis inhaler, or any of the inhalers in common use, is efficient and convenient.

In administering ether or chloroform the general technic is very much alike, and yet there are some very important differences which should ever be kept in mind. Chloroform is much the more powerful anesthetic and more depressing upon the circulation; it requires much less to produce complete anesthesia; it is not exhaled from the lungs as rapidly as ether, because its point of greatest evaporation is higher; it must be administered with a much freer admixture of air, and more cautiously; its dangerous effects are manifested more suddenly, without premonition, and arise frequently in the first stage of anesthesia. The primary effect of chloroform is upon the heart and circulatory nervous centers; secondarily it paralyzes the respiratory nerve-centers also.

In administering chloroform or ether, the anesthetizer must not only watch the heart, but also the respiration, the pupil, the corneal reflex, and the countenance—from the beginning of the anesthesia until the patient is restored to consciousness. Both an-

esthetics should be administered slowly and cautiously so that the respiratory tract may become accustomed to their presence. I am sure that many dangers of anesthesia may be avoided by not pressing the agent too rapidly in the first stage.

In private practice the anesthetizer is frequently embarrassed by the apparent anxiety of the family and friends who may be present; they become nervous if the patient does not yield as speedily as they think he ought, asking every few minutes if the patient is not a long time getting under it, or, don't you think you are giving him too much? As far as possible exclude everybody from the operating-room, except the surgeon and his assistants.

Some minor surgical operations requiring but a moment may be performed during the first stage of anesthesia—that short period of insensibility and quiet which precedes the second stage or stage of excitement; but operations of any gravity should not be begun until the patient is thoroughly anesthetized, because of the danger of fatal syncope from reflex inhibition of the heart.

In inducing anesthesia by ether, in the first stage we should use the drop-by-drop method of administration. The inhaler should be charged with a small quantity of the ether, then held several inches from the face, and the patient directed to inhale cautiously. This distance should be maintained, allowing a free admixture of air, until the respiratory tract has become accustomed to the presence of the anesthetic. The ether is added every few seconds, drop by drop, while the inhaler is brought nearer and nearer to the face of the patient. If the patient coughs, strangles, or resists, the inhaler should be removed until the breathing becomes natural, and the resistance ceases, and then brought nearer again. During the stage of semi-consciousness and non-resistance, the inhaler should be brought down close to the face, the ether added freely, saturating the patient with the anesthetic as rapidly as possible. This process shortens the second stage of anesthesia, which is always accompanied by excitement and resistance.

During the second stage add the ether as may be required, keep the inhaler close to the face, admitting no air except that which is admitted with the ether. If the patient stops breathing, the muscles become rigid, and the jaws clinched, withhold the ether for a few moments until the patient begins to breathe naturally, then push it again, thus cautiously, but continuously. Press the admin-

istration, watching the respiration, the pulse, the countenance, the pupil, the corneal reflex, until the patient becomes unconscious, insensible to pain, and the muscular system is completely relaxed. The ether snore is a pretty good guide as to the completeness of the anesthesia. If the respiration now becomes stertorous, depress the chin with the fingers, and with the thumbs behind the angle of the jaws draw the tongue forward; notice the pupil at this stage of the anesthesia and you will find it contracted and the corneal reflex almost abolished. Many surgical operations can be performed without carrying the anesthesia further.

Push the anesthesia one step further, the corneal reflex will be abolished, the pupil will begin to dilate, the respiration will become noisy—this is the stage of complete surgical anesthesia; the patient is close on the danger line and should be watched with the greatest caution. The skilled anesthetizer is the one who can hold the patient just at this point, while he undergoes the most serious surgical procedure; it requires but a small amount of the anesthetic administered now and then to do this.

Sudden dilatation of the pupil when the patient is profoundly under the anesthetic indicates serious danger, and should be met by the immediate withdrawal of the anesthetic and the admission of air and the use of other means if required. Sudden dilatation of the pupil may, however, simply indicate that the patient is passing from under the effect of the anesthetic. It requires no little tact at times to discriminate between these conditions.

It requires a longer time to anesthetize a patient with ether, and you will have more resistance, but the greater safety abundantly repays you for your trouble. I exceedingly doubt whether any patient who was a proper subject for ether anesthesia ever succumbed under this agent, unless there was faulty administration upon the part of the anesthetizer.

A comparatively safe and pleasant method of anesthesia is practised by many surgeons, and I frequently resort to it, unless there is some contraindication: Chloroform is administered during the first stage of the anesthesia, until the patient is partially unconscious, non-resisting, then ether is substituted and the narcosis pushed to completion with this agent. In this way you get rid of the disagreeable and suffocating feeling which accompanies the first stage of ether anesthesia and which patients so much dread.

The method of administering chloroform as an anesthetic is very much the same as with ether, the drop-by-drop method must be more closely adhered to, the anesthetic must be pushed more cautiously, keeping always in mind the fact that chloroform when administered with a free and full admixture of air is comparatively safe; if administered with exclusion of air it is exceedingly dangerous, and if the anesthesia is prolonged it will certainly be fatal in its results. I lay down this principle as a safe guide in administering chloroform.

Anesthesia by chloroform should be induced and maintained with the least possible limitation of the natural volume of air; the heart's action, the respiration, the corneal reflex, the pupil, must be more closely watched than in ether anesthesia; and with the first danger-signal the anesthetic must be withdrawn and the patient allowed fresh air.

Indeed, the secret of administering any anesthetic is this: produce and maintain the anesthesia with the least amount of the agent possible; keep ever in mind that the danger lies in giving too much of the anesthetic and too little air. In oxygen gas, or better still, in pure fresh air, we have the most complete antidote to the dangerous effect of either ether or chloroform. It is worth more than strychnin, digitalin, nitroglycerin, nitrite of amyl, artificial respiration, electricity, etc.

The fact that pure air inhaled into the lungs is the great antidote to the danger of general anesthesia makes it exceedingly important that we watch the respiration. I am aware that, theoretically, chloroform kills by the heart, while ether kills by the lungs, yet I must say, if I had to choose one single indication as a safe guide in the administration of general anesthesia by any agent, I would most certainly select the respiration. In my judgment it is by far the most important single function to keep under observation; for so long as the respiration continues, we have a means by which we may convey air to the lungs, which is the great restorer. If, however, the respiration ceases, the patient must speedily succumb unless artificial means are resorted to. Ever keep this in mind, embarrassment of the respiration is the most important danger-signal; whenever it becomes seriously impaired admit air at once. You may lose your reputation as an anesthetizer by following this advice, but you will not lose your patient.

An experience of thirty-five years in the use of anesthetics (and I am happy to say, without a single disaster, but with many a scare) has impressed me deeply with the belief that the majority of patients (who are really fit subjects for general anesthesia) who die under its effects are really drowned by the agent, a sufficient amount of air not having been admitted with the anesthetic. Safe anesthesia by any known agent, in my estimation, is only compatible with a free admixture of air. Those of you who have followed me in this address cannot fail to see that the burden of my plea has been air!

But we must admit that so long as our knowledge is in its present imperfect state and so long as human judgment is fallible, danger and disaster may come to even the most skilful anesthetizer; when it comes, do not lose your head or become terror-stricken and abandon efforts to resuscitate your patient. Use the methods and means so well known to all, use them systematically, persistently. It is a terrible moment of suspense when the heart stills, the pupil dilates, and the respiration ceases, but you must be resolute, imperturbable.

Digitalin and strychnin, nitroglycerin, or nitrite of amyl should be used immediately; the windows should be thrown open, the patient's head lowered, the tongue drawn out, artificial respiration resorted to, oxygen gas administered, and electricity used over the precordial region, if thought necessary. Do not abandon your efforts too soon; we have all seen persons seemingly brought back to life after hope had been abandoned.

No doubt the question has already arisen in your minds, Shall we ever find a perfectly safe anesthetic? I, for one, confidently believe we shall, and those of you who live another quarter-century will witness the solution of the question. Whether the solution will come in an improved method in administering those agents we already have, or whether the laboratory will furnish us an entirely new and safe agent, I am unable to say, but the solution will come, and with it the golden era of surgery.

ASEPSIS AND ANTISEPSIS

A CLINICAL LECTURE DELIVERED AT L'HÔTEL DIEU, PARIS

BY PROFESSOR LUCAS-CHAMPIONNIÈRE

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GENTLEMEN: I had occasion, at the recent meeting of the French Association for Surgery, to deliver an address in which I discussed the principles that underlie the application of, and the benefit to be derived from, asepsis and antiseptics in surgery. These principles are so important in the ordinary practice of surgery, especially in minor surgery, such as you will do in the early years of your practice, that I think it worth while to give you the important points necessary for the proper understanding of this very practical subject.

There is no doubt that in abdominal surgery there is a large field for the application of genuine asepsis. The less antiseptics are employed in the peritoneal cavity the better. The successes obtained by the gynecologists who first undertook to remove ovaries were the result of special care with regard to cleanliness. In this matter these original operative gynecologists differed completely from the surgeons of that day. Scarcely necessary to say the surgeons were almost completely neglectful of what would now seem to be even the ordinary rules of cleanliness. The success of peritoneal surgery without antiseptics, however, should not lead us to conclude at once that asepsis is the ideal condition to be maintained and striven for in all surgery. The principal reason for the success of aseptic abdominal surgery is not quite so much the fact that absolute asepsis is always obtained as that the peritoneum has a quite marked tolerance for germ life—even of a virulent character, if too large a number of germs are not placed in it at one time. Not only this, but the peritoneum is able to dispose of substances that would hinder the success of surgery in other parts of the body. Portions of meat, for instance, that have been placed in the

peritoneal cavity of animals are absorbed. This is true even though the pieces of meat are not previously completely sterilized.

There are times, however, when even in the peritoneal cavity aseptic surgery does not fulfil all the indications of the case. If the lesion in the peritoneal cavity has become septic or if because of trauma a large amount of wounded surface is exposed, in addition to rigid asepsis at the time of the operation, at least drainage will have to be instituted in order to secure the peritoneum against subsequent evil effects.

Once outside of the field of the surgery of the peritoneum aseptic surgery loses most of its advantages. Failure to use antiseptics is almost sure to disturb the regularity of the healing process. In certain regions of the body, where there is a special liability to the development of septic conditions, the attempt to apply only the principles of aseptic surgery may lead to serious results.

Modern surgery owes the main part of the progress that it has made in the last forty years to the use of antiseptics. Antisepsis provides not only for defence against known germs that may be present, but also against many accidental infections without germs. To do away with antisepsis is to relapse into some of the old uncertainty with regard to the course that wounds may take, since the invasion of germs cannot always be foreseen and provided against and possible infections may take place. A surgeon who is usually especially fortunate will find his peace of mind disturbed by an accident which recalls to him the necessity for surer protection.

Especially is this true with regard to the surgery of joints. To my mind, joint surgery constitutes the criterion by which we are able to decide that it is impossible to continue surgical practice without the use of antiseptics. It would be easy to recall to you to-day serious results that have occurred as the result of failure to use antiseptics in such simple operations upon the joints, as, for example, suture of the patella. Stiffness of the knee-joint and even death have occurred under these circumstances. The more one takes up the idea of purely aseptic surgery the more will he find that such accidents become frequent.

As far as I am concerned I may say at once that I have never encountered that reputed irritation of the synovial membrane produced by antiseptics which is put forward by so many surgeons as an objection to the free use of antiseptic solutions in joint surgery.

Experience has shown me besides that this irritation occurs only in the practice of those who do not know how to make proper use of antiseptics.

It may be said that the only way we can decide with regard to the use of asepsis or antiseptics in the treatment of wounds is by collecting statistics of many surgeons. Now, statistics may be a source of very valuable information. It must not be forgotten, however, that in surgery particularly statistics are capable of very varied interpretation. It was comparatively easy to urge the introduction of antiseptics on statistical grounds. Antiseptic surgery provided conditions in which the mortality was always almost completely done away with, while in pre-antiseptic days everything was uncertain and the mortality was almost without limit.

Even with regard to antiseptics it must not be forgotten that experience in the use of its principles enables a surgeon to reduce very materially his mortality and his morbidity in any given class of operations. With antiseptics, then, experience plays an extremely important rôle. It is not so much the proper use of antiseptics as the knowledge and practice of the rules of antiseptics that reduces mortality and morbidity. I shall take just two examples from statistics of my own operations in order to show how much carefully applied antiseptics can accomplish in this way.

One of the operations that I have most frequently performed during the last twenty years is that for the radical cure of hernia. I have never attempted the radical cure of hernia by some merely external procedure. For me the operation has always been an absolute laparotomy. In my statistics are included not only inguinal and umbilical hernias, but also ventral hernias of various kinds, some of them being of very large size and requiring very extensive operation. Altogether I have treated over 1000 cases of non-strangulated hernia. The mortality for this number of cases has been less than 0.7 per cent.

I may say at once that this mortality must certainly be considered small, especially when it is remembered that I was a pioneer in doing this sort of work. When I first began to do radical operations for hernia, a number of my colleagues thought such operations almost unjustifiable. I did not have the experience of surgeons in the same line of work to guide me, and most of the patients that came, especially at the beginning of my career, were in a much more

serious condition than are those ordinarily met with at the present time. Nowadays operation is advised by the attending physician before the hernia has become very large or intractable.

Altogether only 7 patients died as the result of the operation. One of these was a case of very severe and unusual epigastric hernia. Another death took place in a bad case of ventral hernia. Altogether there were only 5 deaths in the treatment by radical operation of 868 cases of inguinal hernia. If to these are joined the number of crural or femoral and umbilical hernias, altogether there were 5 deaths in 988 cases, or scarcely more than 1 for every 200 patients operated upon. I may add that none of these cases died because of peritoneal septicemia. All of the deaths were due to some pathologic lesion existing before the operation which had either not been discovered or the significance of which had not been realized. With my wider experience of the present day, I would certainly not have operated in 2 of the cases at all. On 3 of the patients who succumbed to the operation I had refused to operate several times, until their insistence and their declarations that their discomfort justified them in taking the risk overcame my scruples.

If I consider the operations done only on young subjects, most of the patients being young military men, I find that out of 320 cases operated upon there is not a single death. That is to say, the operation for the radical cure of hernia in young, selected subjects has been entirely without mortality. To show, however, how much assurance experience in the use of surgical methods gives, I may say that in my last series of 285 cases, taken as they come, no death occurred.

This, then, is the result of my experience in peritoneal surgery. I do not believe that we can improve much on the mortality from abdominal operation by any new method. At the present the mortality is practically nil. I see no reason, therefore, why I should adopt any other method than the simple practice of careful antisepsis that my experience has taught me to use in these cases. It does not seem to me that the most scrupulous asepsis could give me any better results. Needless to say antisepsis in hospital practice is much easier and less exacting than the absolute asepsis which is the only thing that could replace it.

There is another set of statistics, however, in my surgical expe-

rience of the last twenty years that is even more conclusive with regard to the usefulness of antiseptics as compared with asepsis than even the results of hernial surgery. These statistics are those of my operations upon joints. During the last twenty years I have made 110 resections of the knee. When I began to do it, I had gradually to elaborate my own technic, for no other surgeon was doing the work. You will find no set of statistics among French surgeons, except those of Jules Boeckel, that go back as far as my own. Twenty years ago resection of the knee was an operation that gave the highest hospital mortality. Of these 110 operations I have not a single death recorded as due to the operation. Two patients died five months after the operation, but none at a time any nearer than that. One of these fatal cases was due to pulmonary tuberculosis and the patient had been greatly benefited in his general condition by the operation. The second patient died at the end of five months, from the accidental contamination of a fistula of the soft parts at quite a distance from the knee. At the time of the fatal termination he had been for some two months walking around.

As a matter of fact there was no operative mortality and no infection of the surgical incision. Needless to say in most of these cases the tissues had been previously infected, yet the use of antiseptics proved a sufficient guarantee against the spread of this infection. A like set of results was obtained also in the resections of other joints made during the last twenty years. These resections have included 15 of the shoulder, 47 of the elbow, and more than 10 of the wrist. In none has there been death from infection or suppuration. In a young child operated upon for tuberculosis of the elbow death took place the day of the operation, but was due to a previously unrecognized diffuse pulmonary tuberculosis. In a man operated upon for tuberculosis of the elbow death took place two months later from pulmonary tuberculosis. The operation in itself, however, had nothing to do with these deaths, and no death occurred outside of these.

These statistics show you that when an antiseptic operation is done on the large joints death may occasionally take place, but is rare and does not result directly from the operation itself. It will be very difficult, it seems to me, for the adherents of aseptic methods of surgery to show better results than these as far as regards the

mortality, and I await their statistics with interest. Admitting, however, for the sake of argument, though the proof of it has never been furnished, that operative methods without antiseptics are as successful as regards mortality of the operation as those done under antiseptic precautions, this of itself would not be sufficient to justify completely the exclusive adoption of aseptic methods. Asepsis may prevent primary infection and so preclude death or immediate suppuration. But something more than this is necessary.

We must not only be guaranteed against primary and immediate suppuration, but the operative procedures should successfully protect the patient against secondary suppuration. Secondary suppuration is extremely rare when the antiseptic method is employed, and when it does occur, we know that it is always due to negligence, and this negligence can, as a rule, easily be traced. As Lister said long ago, when suppuration ensues the fault in antiseptic precautions must be looked for.

In spite of the multiplication of scrupulous aseptic precautions, secondary suppuration, as a rule not of very serious character, frequently takes place. In hospital surgery such accidents are occasionally almost inevitable. In order to avoid them it would be necessary to remove the patients entirely from the neighborhood of other patients suffering from suppuration. Surgical wards would have to be divided, and as soon as suppuration occurs, patients would have to be segregated. Even this procedure, however, annoying as it would be, would not suffice for the prevention of possible infection.

This would involve the loss of some of the advantages that were gained for surgeons by Lord Lister's discoveries. What Lister secured for surgery was the possibility of doing operations without mortality and without subsequent suppuration in every place and without the necessity for immense architectural provision in order to segregate possibly infective patients from all others. Antisepsis secures these advantages. To abandon the antiseptic method under these circumstances is to take a decided step backward.

But perhaps the new aseptic method has certain accessory advantages. Perhaps it is more simple and easy, less costly, more conformable to normal conditions, and more economical for use, especially in hospitals. On the contrary, this new aseptic method has any number of complications. I can scarcely help being struck

by the facility with which surgeons of the present day submit to the difficult conditions required for asepsis, when I recall the bitter criticisms that met us years ago when we attempted to introduce the most simple antiseptic manipulations. Surely many of you remember with how much opposition the introduction of the antiseptic spray was greeted. Despite the extremely rigorous prescriptions required for asepsis, no objection seems to be made. It may be said, however, that the difficulties of the antiseptic method are so slight that they can scarcely form a subject for objection.

With regard to aseptic precautions, I shall not insist on the difficulties encountered in the provision of gloves, of masks, and of the enormous quantity of accessory articles demanded, in addition to the care needed in the preparation of the operating-rooms and of the patients. Beyond these, moreover, surgery without antiseptics can be practised only in specially constructed amphitheatres. Notwithstanding the immense expense undergone in the construction of aseptic operating-rooms, we are told that those in use at the present day are already behind the age, and that new ones must be built.

Every detail is becoming more and more difficult to master. Take the extremely small detail of suture material. For thirty years, now, surgeons have been exercised over the question of the famous aseptic suture. One eminent surgeon declared not long ago that suture material that was perfectly aseptic at the beginning of an operation might become septic before the end, simply because of the prolongation of the operation. As for myself, I have never had any difficulty about suture material. I have always employed the same sort of catgut, prepared by the original method suggested by Lister, with the single addition of a bath in a strong antiseptic solution—the essence of turpentine—and I never subject my suture material to any other form of sterilization. I have never had any trouble from the use of this catgut. I have used it very freely; and while other surgeons have been complaining of the impossibility of obtaining suitable suture material, I have never had any anxiety. The only reason for the differences between our states of mind is the fact that I used antiseptics freely while they did not.

For the last thirty years, then, whenever surgical practice has departed from the great theory of Lister we have been warned of the fact by surgical mistakes and consequences which have proved

fatal for many patients. It is not only in surgery, however, that the use of antiseptics has proved of the greatest service. Being an obstetrician, I was one of the first to show in France that obstetrical practice could and would be benefited by the introduction of antiseptic precautions. In my obstetrical practice I used exactly the same principles as in my operations and in my antiseptic dressing. I said that uterine and vaginal lacerations, when once sterilized by the application of an antiseptic, do not require repetitions of the antiseptic wash any more than any surgical wound. I forbade all secondary injections, because they constitute an abuse of true antiseptic principles.

As in surgery, the antiseptic method in obstetrics became modified in the course of time. The first modification was the adoption of a solution of sublimate as the antiseptic fluid, instead of a solution of carbolic acid. Sublimate, because of its tendency to be precipitated by albuminous substances, is only a very mediocre surgical antiseptic. Because of its poisonous qualities it is a positively bad obstetrical antiseptic. Because of the general introduction of sublimate solution into obstetrics the injections were varied and multiplied to excess.

The present condition of obstetrical statistics shows you the result of these modifications of the original simple obstetrical technic I suggested. As a matter of fact the results in obstetrical work in private practice are more unfavorable than in hospital practice. This unfortunate state of affairs depends on the too frequent application of useless injections. An injection made with a mediocre antiseptic, or with a substance that is simply sterilized, constitutes a bit of technic in obstetrical work that is essentially dangerous and extremely difficult to keep under proper surveillance. As a consequence one sees, even in good conditions in city practice, a series of puerperal accidents. Needless to say these are infinitely less in hospital practice than they used to be.

I may add that I have at the present moment the satisfaction of knowing that a considerable number of obstetricians now deprecate the use of secondary injections. They are returning to practical methods in obstetrics, much more in conformity with my original practice in the matter, and more nearly in accord with antiseptic doctrines as laid down by Lister. I am of the opinion that surgeons will do the same thing before long. The difficulties of surgical prac-

tice without antiseptics and the irregularity and uncertainty of its results will bring surgeons back to the regular employment of chemical antiseptics.

It may be said that it is a great presumption on my part, just as present-day surgery is taking up more and more the question of expensive installation and carefully arranged operating-rooms, to proclaim that surgery is surer when done with antiseptics. It will be said that the uselessness and the danger of employing antiseptics are constantly proclaimed in France and abroad. There would seem to be almost a consensus of opinion on these points. I may say, however, that I am not unaccustomed to find an almost unanimous opinion against me, and that I am not accustomed to be very much disturbed thereby. By a sort of fatality I have not infrequently had to combat public opinion, not only with regard to antiseptics, when it was being originally introduced, but in a number of other important questions.

When I suggested the more frequent use of the trephine than was formerly the custom I met with violent opposition. When I suggested that cerebral localization might be made of avail to enable the surgeons to relieve intracranial conditions I was almost laughed at. Even Broca himself was not ready to admit that cerebral localization could be of any practical service except with regard to aphasia. Needless to say there is no opposition with regard to my views on these questions at the present time. I had practically the same opposition to overcome with regard to the radical cure of hernia. Many of my esteemed contemporaries who practise it very freely at the present day scarcely thought it justifiable when I first began to recommend and practise it. In fact at the present moment the radical cure of hernia is universally accepted as the indication wherever hernia exists in young people, or is not easily controlled by a truss, or is producing discomfort. There are even cases of hernia giving such slight symptoms as to be scarcely noticeable in which some of my colleagues recommend the performance of radical cure, but in which I think it scarcely justified. I have begun to counsel moderation in the matter.

It is more than twenty years now since I first began to recommend mobilization in the treatment of fractures. Not a few attacks have been made upon the method, but I have not been disturbed by them. I have not permitted myself to be turned aside from the prac-

tice of a method of treatment which from personal observation I found to be beneficial, even though according to all the accepted doctrines of surgery it seemed paradoxical.

With the realization of these differences of opinion clear in my mind, I recommend a return in our present-day surgical methods to the doctrines of Lister. Antisepsis should be the watchword rather than asepsis. Surgery will not be successful without the use of chemical substances which act as germicides. The microbic enemy is too manifold and too subtle. It is true that suppuration does not take place wherever there are no infective germs. But in the absence of antiseptics the removal of germs cannot be assured. According as cleanliness and the perfection of surgical technic remove opportunities for infection the chances of suppuration occurring are very much reduced, but they are never entirely removed. This method, without antiseptics, can never improve surgery unless it gives the absolute guarantee against infection which properly perfected antisepsis provides.

If we wish to be assured against all intrusion of septic material and of irritating substances, natural or accidental, we must have recourse to antiseptics, because it is necessary that the enemy should be destroyed as soon as he presents himself. If you wish to have surgery without danger, no matter what may be the surroundings and the condition of the poor people among whom the operation is performed, you must have recourse to surgery with antiseptic precautions. Moderate the amount of antiseptics employed. Diminish the number of washings with the antiseptics, limit as far as possible even their possibilities of local irritation—this is the work of true progress in surgery.

After so many years carbolic acid still holds its position as the most simple and the most favorable of antiseptic substances. There are many other chemical materials with which surgery can be accomplished in safety. In fact the number of such materials is almost limitless. In practice, however, we must limit ourselves to certain very simple materials. For my own part, considering the advantages and the absolute simplicity of the use of carbolic acid, together with our widely extended knowledge with regard to this substance, it seems to me that its further use and study would be more surely useful than attempts to discover other materials that will have perhaps less advantages.

With regard to surgical practice, then, it seems to me that advance in surgery is dependent on certain great principles. These may be stated about as follows:

We must practise moderation in the use of antiseptics in the surgery of the internal viscera, the intestines, the stomach, and the liver. In these organs antiseptics are at once less useful and liable to do more harm than in most other operations. As soon, however, as there is the slightest danger of the intrusion of septic material, then laparotomy must revert to the domain of antiseptic surgery. For all operations outside the abdomen, antiseptic surgery provides the simplest and surest method. For hospital surgery antiseptics is the only method which sufficiently guarantees against infective accidents, so as to affirm definitely the absence of danger in all surgical procedures.

For myself, at the present moment the use of carbolic acid as an antiseptic takes the first place. Besides this, I believe that hydrogen dioxid and in a certain measure iodoform, are very desirable chemical substances for use as antiseptics. Of course, in addition to these substances, fluids that are employed and materials that come in contact with the wounded tissues must always be sterilized.

I do not wish to be more Listerian than Lister, however, and so I am ready to admit that in antiseptics any substance is valuable only as far as it is a germicide. It may well happen, then, that chemical discoveries in the very near future will provide for us certain substances more powerful as germicides and more favorable in their lack of irritating properties than any that we at present possess.

The employment of absorbable suture material, the useful rôle of drainage in wound-dressing, the necessity for compression, and the other accessory indications of the method of dressing wounds pointed out by Lister remain to my mind as valuable suggestions to-day as they were when originally given by the greatest surgical genius of the last century. The rules he has laid down are intimately bound up with the theory of the healing of tissues which he formulated so perfectly and which no subsequent theory has as yet been able to replace.

GASTROSTOMY; CONCUSSION OF THE BRAIN

A SURGICAL CLINIC HELD AT THE MEDICO-CHIRURGICAL COLLEGE HOSPITAL,
PHILADELPHIA

BY WILLIAM L. RODMAN, M.D.

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GASTROSTOMY

GENTLEMEN: The first patient that I shall show you to-day is one upon whom I shall perform gastrostomy on account of a carcinoma of the esophagus. The patient is a man, aged 38 years, who has difficult and painful deglutition, and has lost about 30 pounds during the past year. These, together with other symptoms and the results of a careful physical examination, have warranted a diagnosis of carcinoma of the esophagus.

Stricture of the esophagus may be either spasmodic, fibrous, or the result of malignant disease. In this case you will almost immediately rule out spasmodic stricture, as it is generally met with in hysterical women, very rarely in men. Fibrous stricture may result from many causes, such as the swallowing of carbolic acid or other corrosive poison, or it may result from syphilis, traumatism, or benign tumors. Malignant stricture is due to malignant disease, and the one form of malignant disease that is frequently found in the esophagus is epithelioma of the squamous-cell variety.

We are reasonably certain that this is a malignant stricture, notwithstanding the fact that the man is only 38 years old. In looking over the literature yesterday, I found the statement that malignant stricture of the esophagus never occurs prior to the fortieth year. The present case serves to illustrate the truth of what I have stated here time and time again, that malignant disease is breaking down all barriers that have hitherto been thought to exist. The man whose penis I recently amputated, and who is only 30 years old, is the youngest subject that I have ever seen with this condition; and this man is certainly the youngest patient, by 5 years, that I have ever

seen suffering with malignant disease of the esophagus. Thus we are made to realize that malignant disease is increasing. It seems that almost everything that we have had at this clinic during the last month has been malignant disease: malignant disease of the breast; of the jaw; of the parotid gland; of the lip; of the tongue; everything, it seems, has been malignant disease.

This man has been afflicted for some time. The stricture is so tight that it will not allow the passage of a tube the caliber of a lead pencil.

Stricture of the esophagus may be situated at any point throughout the length of the tube, and it is a matter of great importance to determine the exact location. In the first place, it is very apt to be opposite the cricoid cartilage, and we think that is the location in this case. Possibly the next most frequent site is where the lumen of the esophagus becomes narrowed, as it passes behind the left bronchus. Then again we find malignant disease of the esophagus at the cardiac orifice of the stomach.

How will you tell where the stricture is? You pass a flexible sound or tube through the esophagus until it meets with the resistance caused by the stricture; you then mark with your thumb that part of the tube at the entrance to the mouth, withdraw the sound, and measure the distance to the tip. The distance from the mouth to the stomach is about 18 inches; thus by subtracting from 18 the number of inches that the tube can be inserted, you can tell how far the stricture is from the stomach. If the tube goes in 14 inches you will know the stricture is very near the stomach. If, on the other hand, it goes in only 4 inches, you will know it is near the cricoid cartilage. If it goes in 8 to 10 inches, the chances are that it is behind the left bronchus. Metal bougies are dangerous and should be used with the greatest caution, lest perforation result.

How will you treat strictures of the esophagus? Hysterical strictures are treated by the administration of antispasmodics, and by dilatation. Fibrous strictures will be overcome by dilatation in many instances. Treat upon the same principles that you would treat a urethral stricture. At times it will be necessary to cut it internally—esophagotomy—just as you would perform urethrotomy. This is often dangerous, and should not be undertaken lightly. The treatment of malignant stricture is entirely different from that of the fibrous variety. Here dilatation is manifestly out of place,

for by dilatation you would be stimulating the malignant growth to increased activity, to say nothing of the dangers of perforation. The only treatment that avails anything in malignant disease is to perform the operation that we will do to-day, known as gastrostomy. Gastrostomy means simply cutting into the stomach, while gastrotomy is the establishment of a mouth or permanent fistula through the abdominal wall. By this operation the man's life can be prolonged, for if we relieve the tumor in the esophagus from the irritation caused by the passage of food, and feed the man through this artificial mouth, undoubtedly we will stay the progress of the disease to a very marked degree.

There are many ways of doing the operation of gastrostomy, as those of you who have taken the course on operative surgery know. The operation which enjoys the confidence of the profession at large, and, I think, all things considered, is being done more frequently than others, is the Franck-Ssabanajew operation, introduced nine years ago. The operation next in popularity is that of Witzel. The methods of Howse, of Senn, and of Hahn are also sometimes practised. The operation which I usually attempt, and I say "attempt" advisedly, is the Franck-Ssabanajew operation. For the successful performance of this operation the stomach must be freely movable, and $1\frac{1}{2}$ inches of the organ must be drawn out of the abdomen through the incision; otherwise it cannot be done. If I find the stricture is at the cardia in this case, and the stomach bound by adhesions, I will have to abandon any attempt in this direction, and perform the Witzel or the Senn operation. Believing, however, that the stricture is high up, somewhere in the gullet, and that there should not be any adhesions of the stomach, I hope to be able to withdraw it successfully. Yet I know very well that because of the stricture the stomach has not for a long time been distended by food to its normal capacity, and that therefore it may have become atrophied. Occasionally the stomach may hide itself behind the liver and be found with difficulty, if at all. I will really do the Kocher modification of the Franck-Ssabanajew operation, which I think is better. In Kocher's modification, instead of making an oblique incision parallel with the costal margin, the incision is commenced in the substance of the rectus muscle, the advantage being that the fibers of the rectus are separated, the stomach brought out, and when the operation is completed the rectus muscle acts as a true

sphincter and prevents leakage of the stomach contents, on the one hand, and excoriation of the skin from leakage, on the other hand.

Having now made my incision, $1\frac{1}{2}$ inches from the median line, beginning opposite the eighth costal cartilage, I come upon the rectus muscle. I cut the sheath and then separate the fibers. I now cut through the posterior sheath of the muscle and the peritoneum, and pass my finger into the abdominal cavity, over the lower margin of the liver to the region where the stomach ought to be. I find that it is in its normal position, free from adhesions, and, as you see, I can readily bring out a portion of it through my incision. One might very easily mistake the transverse colon for the stomach, and care must be taken in this respect. The stomach, however, should be easily recognized by its blood-vessels, the thickness of its walls, and its pinkish color. The opening into the stomach should be made near the greater curvature in the vicinity of the cardia, as in that way regurgitation will be avoided. We can see the blood supply very well and thus avoid injuring a vessel. The stomach is movable and can be extruded. I shall therefore complete the operation in what I think is the ideal way. I draw out a cone of stomach, about $1\frac{1}{2}$ inches long, and suture this carefully, all the way around, to the parietal peritoneum and the posterior sheath of the rectus muscle, being careful to pass the sutures only through the serous and muscular layers of the stomach. I will use the continued suture in this case, as it is quicker and just as satisfactory. This part of the operation, as you see, is at best quite tedious. By suturing the stomach to the peritoneum all the way around I promote adhesions between the two surfaces. This same principle is made use of in many other operations. The same thing is done in colostomy; the colon is brought out and sewed in the same way that I am doing now, so as to promote adhesions which will be firm and prevent leakage into the peritoneal cavity. Another important point in gastrostomy is to have the stomach washed out before operating. In this case it was impossible on account of the tight stricture of the esophagus, but we did the next best thing, and kept it empty for from six to eight hours. It is also important to prevent vomiting, if possible, after the operation, and we are giving this man chloroform instead of ether, on that account, for, as I have often told you, chloroform is less apt to be followed by vomiting.

I would like you now to recall the anatomy of these flat mus-

cles. At this part of the linea alba, the upper three-fourths, the internal oblique muscle splits into two layers, the posterior layer going behind the rectus and forming its posterior sheath, and the anterior layer passing in front and forming its anterior sheath. It is the posterior sheath that I am now including in my sutures along with the parietal peritoneum. The transversalis joins with the posterior sheath and the external oblique joins with the anterior sheath. Formerly this operation was done in two stages, as it was not considered safe to open the stomach at the time of the first operation; by the modern method, however, this is perfectly safe. The thought may occur to you, Why not remove the esophagus, if it is the seat of malignant disease? This has been attempted by Billroth and others, but no one at the present time would call this judicious surgery. I will tell you next week, when lecturing upon malignant disease, that it is a surgical tenet to let the tumor alone unless you can remove all of it, for partial removal stimulates the growth and causes it to develop in an unwonted manner. I am very enthusiastic about certain operations for malignant disease when I can get out all diseased tissue, and I have reasons to make me so. I have seen patients live many years after the operation for cancer of the breast, penis, lip, etc., and I believe them permanently cured. A free dissection so as to insure success is impossible in malignant disease of the esophagus.

Having now finished the suturing, we will make a second incision about 1 inch long, $1\frac{1}{2}$ inches above the first incision, penetrating only the skin and subcutaneous tissue. I now undermine, with my finger, the intervening tissues, making a subcutaneous connection between the two incisions, and through this space I draw the tip of the extruded stomach. You see now why I said we must withdraw $1\frac{1}{2}$ inches of the stomach from the abdomen. Having now drawn the tip of the cone through this second incision, I sew up the original incision. We will now open the stomach at the tip of this cone, and the operation is practically over. As I said before, the fibers of the rectus will act as a true sphincter to the stomach, and this is why I prefer this modification rather than the original Franck-Ssabanajew operation. Kocher is a great anatomist, and advises making what he calls "normal incisions" where practicable, incisions that interfere very little with the integrity of the tissues cut through. There is less danger of cutting a nerve by this

method, and less danger of ventral hernia. I now place this catheter in the stomach, and will allow it to remain there until we have a permanent fistula established. We will introduce no food into the stomach for 24 hours. We could feed him now if he were much reduced, but it is never desirable to feed patients after abdominal operations for 24 or 36 hours. The great mistake that is made in this operation is that it is usually done too late. It is postponed until the patient is in a moribund state.

CONCUSSION OF THE BRAIN

The second patient that I shall show you is this man, aged 55 years, who was injured on January 29 last. A friend of his told us that he was struck on the head by a piece of board, but the patient himself remembers nothing of the accident, having been rendered unconscious by the force of the blow. I was present when he arrived at the hospital,—in a profound state of shock; the pulse was rapid and feeble, respiration irregular and sighing, and his temperature was subnormal. He also showed a disposition to vomit.

An examination of his head revealed an enormous hematoma, the scalp purple, and the tumor well marked. The house surgeon thought that he detected a fracture, and I therefore examined his head very carefully, but was not able to satisfy myself as to the existence of a fracture. On the contrary, I said at the time that there was no fracture, and that the crepitus which was present was due to the hematoma. Within 24 hours the ecchymosis had extended forward, well down on his face, the whole forehead being black from the extravasation of blood. The next morning the house surgeon said: "I think there must be a fracture there, because the patient has been wild all night; his symptoms are exactly like those in a fracture case we had a few days ago."

There is no way to diagnosticate a fracture at the base of the skull except by certain symptoms which were absent in this case. Although his forehead and eyelids were blue, I noticed that his conjunctivæ were perfectly clear; in other words, there was no subconjunctival hemorrhage, and I therefore eliminated fracture of the anterior fossa. If there had been subconjunctival hemorrhage and with it hemorrhage or cerebrospinal fluid or both flowing from the nose, I could not have explained it on any hypothesis other than fracture of the anterior fossa.

His subsequent condition has been most interesting. There has been no rise in temperature, but for two or three days the symptoms were those of a mild leptomeningitis. When he was lying still he was curled up on his side and was inclined to be somnolent, but could at all times be aroused. His bladder and rectum emptied normally for some days after his admission. After the expiration of ten days, however, he seemed to lose control of his sphincters, and his urine was passed involuntarily, as were also the feces. At the same time that this was going on there was a great deal of swelling over the vertex, and the crepitation was well marked. This led several persons to think that there might be a fracture of the vault, but I thought the crepitation was due to the extravasation of blood. There were never any symptoms sufficiently localized to warrant me in trephining. There is at the present time some little paresis of the right side, but no paralysis. I think his grip is a little less on the right side. There was at no time escape of blood and serum from the ears, or hemorrhage from the nose.

Now, gentlemen, I have said enough about the history of this case. It represents a severe type of disorder, of which we see many in this hospital. I had almost a similar condition in a female patient not long ago, and she made a prompt recovery, because she was younger and the injury was presumably not quite so severe. The diagnosis in this case, beyond any doubt, is concussion of the brain; the symptoms were typical of concussion, and that leads me to say that the late symptoms of concussion are very often called "contusion." At the present time the trend is to call all the symptoms, early and late, concussion, and to ignore the term "contusion."

Formerly we divided cases into concussion, contusion, and compression. The word "concussion" would indicate that the brain has simply been shaken or jarred, that there has been a molecular disturbance of the brain, transitory in nature, and that afterward its function has been restored. This passed muster for a great many years, until Duret and Miles proved that in practically all cases of concussion of the brain the tissue is more or less torn; therefore a concussed brain is necessarily a lacerated or contused brain. At the same time that there are minute lacerations of the brain substance here and there, there are apt to be small punctate hemorrhages throughout the brain and at some points these are larger than at others. The authorities just mentioned believed that

the early symptoms of concussion are due to the fact that there is interference with the cerebrospinal fluid, that the impact on the cranium drives the cerebrospinal fluid through the lateral and third ventricles into the fourth ventricle and in this ventricle there is an irritation of the respiratory center, and that this explains the immediate and severe symptoms that we call surgical shock, or collapse. Undoubtedly that is the best explanation that can be given of these early symptoms, but there must also be presupposed an interference with the blood supply of the brain, which is shown by minute capillary hemorrhages here and there and minute lacerations of the brain substance itself.

Felizet also made some interesting observations. He took a skull and filled it with paraffin and let it drop on the floor. The skull was not broken, but when it was opened there was found to be an indentation in the paraffin just below the point of impact, showing that the skull was depressed for the time being, long enough to make an indentation in the paraffin, and then resumed its normal contour. The paraffin, however, remained indented, and if this can happen with paraffin it certainly can happen in the living skull, filled with brain tissue and cerebrospinal fluid. This caused a revolution in the pathology of concussion of the brain, and you will find in many of the recent text-books on surgery, the American Text-book, and Da Costa's Surgery, for instance, that the word "contusion" is not mentioned. A few authors cling to the old classification. I am led to speak of this because at the recent exhibit of the Pathological Society a student from another college whom I knew, and who was interested in the exhibit of the nervous system, said to me, "I see here minute hemorrhages through the brain in a case of supposed concussion. Do you teach that this is the pathology of concussion?" "Yes," I replied; "I have taught that for ten years." The student informed me that such was the teaching of one of his professors, but not of another who held to the old pathology of concussion. So we now explain the pathology of concussion of the brain by saying that it is an interference with the cerebrospinal fluid due to a forcing out of this fluid from the lateral and third ventricles into the fourth ventricle, and the excess in the fourth ventricle acts upon the cardiac, respiratory, and other centers and causes symptoms more or less severe according to circumstances. They are generally more marked and abiding in the aged, less pronounced and more evanes-

cent in the young. Duret showed that while you may have a fracture by *contrecoup*, you can have the same thing taking place with the membranes of the brain without any fracture. There is a "cone of depression" on one side and a "cone of bulging" on the opposite side, due to protrusion of the membranes of the brain caused by the fluid beneath.

The early symptoms of concussion are those we have in this case; pallor, frequent pulse, frequent respiration, irregular and sighing in character, cold skin, patient not unconscious but only able to answer in monosyllables. The senses are obtunded in concussion but not abolished; if spoken to loudly he can hear; he cannot see very well, and yet he can see. The pupils are dilated, perhaps unequally so, and are responsive to light, which is not the case in compression of the brain. The sphincters are usually relaxed, and the patient will empty his bladder and rectum involuntarily. This is almost certain to occur in young children. The temperature is subnormal. These symptoms last for a varying time and usually pass away with vomiting. So vomiting in such cases is usually a pretty good sign, indicating that reaction is taking place. After 24 hours there is no paralysis in concussion, there is no hemorrhage of sufficient extent to make pressure, and of course it is too early for inflammatory exudates to make pressure upon the centers of the brain. Within 24 or 48 hours, as a general rule, the patient complains a great deal of headache, is restless and hard to keep in bed. He always lies on his side, with his legs curled up and his head buried under the covers. The attitude is so characteristic that Erichsen and others have called attention to it from time immemorial. The patient will usually have an elevation of temperature; not high, 100°, sometimes 101° F. Mild cases of concussion will begin to convalesce in 48 or 72 hours. Severe cases are much longer in convalescing. Children will get well much quicker than old persons. The slightest injury to an old man with diseased blood-vessels may easily cause death. The late symptoms of concussion, or so-called "contusion," although I object to the term, may be due to hemorrhages, and as a result of the lacerations and hemorrhage there may be inflammatory exudates thrown out, and we may have paresis of an arm or an entire side due to pressure upon the centers in the brain.

I am satisfied that this was not a case of fracture of the skull.

If there had been a fracture it would almost certainly have occurred at the vault or base, and if we had had a fracture of the vault or the base we would have had different symptoms than we had here. If I had been in doubt as to the existence of a fracture at the time, I would have made a large flap, cut down upon the bone, examined it very carefully with my finger, and if I had found a depression I would have trephined. We thought that on account of this man's age and general condition either chloroform or ether would have been very dangerous, so we decided not to explore the skull, and I am glad we came to this decision. Fractures of the skull are not different from fractures of other parts of the body. The only reason they have a gravity connected with them is due to the fact that there are apt to be lesions of the brain and membranes below. You cannot well fracture the skull without injuring the brain or the membranes.

Fractures of the skull are divided into fractures of the vault and fractures of the base. Fractures of the vault are due to direct violence, and fractures of the base may be due to direct, but more likely to indirect, violence. The patient falls from a distance and alights on his feet or buttocks, and in this way the shock is communicated through the spinal column to the skull, causing a fracture. Fractures of the base are divided into fractures of the anterior, middle, and posterior fossæ. Fractures of the posterior fossa are the most dangerous, and can be recognized by an enormous ecchymosis at the mastoid process. In fracture of the middle fossa there will be escape of blood and cerebrospinal fluid from the ear, and later paralysis of the facial nerve. In fractures of the anterior fossa there are subconjunctival hemorrhage and bleeding from the nose. Fractures of the base, while they are very serious, occasionally end in recovery. You must not conclude because there is hemorrhage from the ear that the patient has a fracture of the middle fossa of the skull, because there may be a ruptured blood-vessel in the auditory canal, a superficial vessel which will account for the blood; but if the hemorrhage is great and is followed by this peculiar serum, not the serum that will follow a blood-clot, but a serum of peculiar color, containing albumin and an abundance of chlorids, possibly a little sugar, and one which comes out more freely if the patient coughs, laughs, cries, or strains—then you know there cannot possibly be any doubt as to a fracture of the base, through the petrous portion of the temporal bone, and rupture of the tympanum.

These fractures of the middle fossa of the skull are necessarily compound fractures, for even if the ear-drum is not ruptured they communicate with the air through the Eustachian tube, and as they are compound fractures they are very apt to be followed by septic meningitis and are therefore very, very serious affairs.

Fractures of the anterior fossa of the skull may take place in many ways. In the first place, a man may fall upon a nail or sharp stick, which will pass into the orbit, nose, or mouth, into the anterior fossa of the skull. Then again they are not infrequently the result of a violent blow on the forehead, and a fracture may extend down through the orbital plate of the frontal bone and in that way cause a fracture of the anterior fossa of the skull. These fractures are also compound, due to the fact that they open into the nose, mouth, eye, and for that reason their treatment must be based upon antiseptic principles. Fractures of the base are desperate affairs, and yet since we have recognized antiseptic principles in the treatment of these fractures the mortality is lower than it was even 10 years ago. By making approximately aseptic the nose, mouth, and throat, the mortality after these fractures is enormously reduced, and now it is not an uncommon thing to see fractures of the base of the skull recover. I have just discharged a patient with undoubted fracture of the middle fossa who was 6 months in convalescing. He still has slight facial paralysis.

There is no reason why we should stop to speak in a didactic way of fractures of the vault, as they are like fractures anywhere else. They are divided into simple, compound, comminuted, depressed, stellate, etc.

Now, as to the probabilities of this case before us. These severe cases of concussion in old men and old women are very, very slow in getting well. Sometimes they never get well. There is a tendency to persistent headache and a want of intellectual vigor and acumen which is sometimes very slow in returning. In an old man like this I would give a very guarded prognosis, for many such patients never get well, and others find their way into an asylum. Headache is a very common symptom, and a man who uses his brain, or leads an intellectual life, should be advised to give up business for weeks or months, take a sea voyage, and allow nature to repair the damage which was done. If you look upon concussion as a simple jarring of the brain, you will not understand the gravity of the condition; but

if you understand and accept the modern pathology of concussion of the brain, you can appreciate that there are serious cases and mild cases, depending upon the pathologic changes that take place at the time of the accident. I do not believe that every case of concussion is followed by a large amount of laceration of the brain. Take a child, for instance, that will roll off a mother's lap onto the floor, strike its head, become pale, vomit, go to sleep, and in a little while will wake up seemingly all right. This is a very, very mild case of concussion, and I can understand that there has been little structural damage to the brain substance, the symptoms of shock being largely due to the disturbance of the cerebrospinal fluid which is forced from one part of the brain to another. But it is utterly inconceivable to me that the symptoms of this old man, which have lasted for weeks, could have been due to any such an evanescent cause. There is necessarily a lesion here, which is undoubtedly due to tearing of the brain rather than simple jarring.

Why do I say nothing about compression of the brain? Because there is no evidence here of compression. If he had had symptoms of compression he would have been unconscious, he could not have been aroused. You may stand over a man and shout at the top of your voice, when he has compression, and he does not hear you. He lies on his back and does not move. The pupils are very widely dilated and are not responsive to light at all. Then again, instead of this rapid, frequent, irregular pulse, you have a very slow, full pulse, sometimes being not more than 30, 40, or 50. Then the breathing, instead of being rapid and superficial, is very slow, deep, stertorous, the latter symptom being due to partial paralysis of the muscles of the face.

There is also paralysis in compression, probably of one side, hemiplegia, or it may be of one extremity only, monoplegia. There may be paralysis of the entire body, but there *is* paralysis, and there is no paralysis in concussion; so there is no reason in the world why one should mistake a pure case of concussion for a pure case of compression. There are frequently "mixed" cases, however, in which there are some of the symptoms of concussion and some of the symptoms of compression.

As to the sphincters, a patient with compression does not void urine involuntarily; there is just the opposite condition, retention, and you have to catheterize the patient regularly.

The bladder may fill up and even burst without the patient having any desire to pass water. The rectum cannot be emptied without the strongest purgative.

A more difficult diagnosis to make, and one we occasionally have to make in hospitals, is the differential diagnosis between compression of the brain, uremia, Bright's disease, and alcoholism or drunkenness. I have been called to operate for compression of the brain when the condition proved to be uremia. In another case it was alcoholism. A man may have a serious injury to the brain and still have the odor of alcohol on his breath. Then again a man who has been drinking may fall as a result of the alcohol and have compression in addition. Therefore the question of diagnosis is of the greatest importance, and one should recognize the necessity for a very careful examination of all such patients brought into a hospital through the accident service.

The treatment of these cases is a most important matter. During the stage of shock everything should be done for the patient's comfort and to insure reaction. All constricting clothing should be at once loosened or removed so as to favor the already greatly embarrassed circulation and respiration. The head should be low, preferably without a pillow. In extreme cases the foot of the bed may be elevated. Artificial heat should be applied by means of hot-water bags and bottles, care being taken of course to wrap them well so as to avoid burning the skin. Alcohol, which is usually promptly offered by some bystander, is distinctly contraindicated in all cerebral injuries. Ammonia by inhalation or the aromatic spirit taken by the stomach produces both a prompt and salutary effect, and is free from the disagreeable and harmful effects of alcohol. Strychnin hypodermically is indicated for its effect upon the cardiac and respiratory centers, and is perhaps the best remedy. It is, moreover, well borne in the profound shock of concussion: $\frac{1}{30}$ of a grain (0.002 gram) can be safely repeated in a half hour. If the patient is able to swallow, a little very hot black coffee may be given; otherwise, it should be given by the rectum. When reaction takes place, usually indicated in children particularly by vomiting, all stimulation should be withdrawn, as there is danger of overaction or inflammation. The patient should be kept in a darkened room and not allowed to talk or see visitors. Bromids and cold to the head best control the cerebral circulation. Opium should

be used sparingly, if at all. Gentle purgation is always indicated, and, in my judgment, nothing acts so well in these cases as calomel given in small doses frequently repeated. It lessens intravascular tension and exerts a derivative effect.

When there is some headache, not controlled by bromids or an ice-cap, I prefer the coal-tar preparations to opium. Leeching is also indicated in some cases. The diet is of the greatest importance. All stimulating food should be withheld. Milk only should be given for the first two or three days.

Possibly the greatest and most frequent mistake made in the treatment of concussion is in allowing such patients to resume work too soon. Any intellectual activity is almost certain to result in headache, insomnia, etc., and if persisted in may result in insanity. A professional man or one who does much brain work should take unusual precautions against indiscretions of all kinds: tobacco, alcohol, overeating, irregular hours are all distinctly prejudicial and should be avoided for weeks or even months if necessary. When one's circumstances permit, nothing does so much good as a long sea voyage. When intellectual work is resumed it should be done gradually.

INTRASCROTAL TUMORS

A GENITO-URINARY CLINIC HELD AT THE RUSH MEDICAL COLLEGE, CHICAGO

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GENTLEMEN: A number of very interesting cases appear before us to-day seeking relief for various lesions located within the scrotum. These five male patients ask for treatment for an enlargement within the scrotum. Here, as elsewhere, intelligent treatment presupposes accurate diagnosis, and the differential diagnosis of a tumor within the scrotum must be based upon a mental catalogue of all possible tumors which may be found in this locality.

An intrascrotal tumor may consist of (1) an enlargement of the various structures normally contained within the scrotum; or (2) it may be due to intrusions into the scrotum of certain abdominal organs.

The first class includes: (*a*) Tumors within the tunica vaginalis, which are either a hydrocele or a hematocele. (*b*) Tumors of the epididymis, which are usually due to one of the three most common infections—the gonococcus, the tubercle bacillus, or one of the many varieties of the pus bacteria. Less often cysts are found. (*c*) Tumors of the testicle proper, the chief among which are syphiloma, cystoma, carcinoma, and chronic orchitis, the latter usually the result of a previous infection by one of the pus bacteria. (*d*) Enlargement of the veins returning from the testicle—varicocele.

The second class of intrascrotal tumors, consisting of dislocated abdominal contents, comprises hernias. The dislocated organ is usually the intestine or the omentum, less often the bladder. Any two or all three of these structures may be present in a scrotal tumor.

Now, I shall ask members of the class to examine these various patients, and I trust that you will bear in mind this list of possible scrotal tumors so that you may make a diagnosis of the conditions

existing by examination before attempting to get any history to corroborate your diagnosis.

CASE I.—Our first patient is a man, 25 years of age, and the scrotal enlargement is very apparent on the right side. The inguinal canal is normally closed, thus excluding the possibility of this being a hernia. The testicle is but slightly swollen, but the epididymis is very much thickened, especially at its lower end (the tail). This fact—that the swelling consists of a hardening involving chiefly the tail of the epididymis—shows us that the enlargement is due to an infection with either the gonococcus or a pus bacterium. By milking the penis we obtain a drop of pus, which on microscopic examination is found to be thickly populated with gonococci. Inquiry elicits the information that our patient contracted gonorrhea four weeks ago, and that the swelling in the epididymis began about eight days ago. The case is therefore a gonococcus infection of the epididymis, or gonorrheal epididymitis.

CASE II.—This second patient is a man, 32 years old. Digital examination shows such a thickening of the right epididymis as to make this organ almost equal in size to the testicle itself. This enlargement is greatest at the upper end (the head) of the epididymis, a fact which characterizes infection with the tubercle bacillus; moreover, the swollen epididymis is very nodular and not smooth, as in the previous case. In these cases of extreme enlargement of the epididymis you must always be careful not to make the mistake of taking the enlargement to be of the testicle. By careful palpation you can readily distinguish the epididymis from the testicle.

When we now come to examine the left epididymis we find that it, too, shows a hard, nodular thickening of the upper part, or head, with but little change in the lower end, the tail. Evidently there is here a more recent and less extensive tuberculous infection of the epididymis.

I want to call your attention in particular to the extremely healthy complexion, good nutrition, and apparent good health of this patient in spite of the tubercular infection of both epididymes. We often find this good general condition with a local tuberculosis of the genital organs. The general impression that a tuberculous patient is necessarily emaciated and cachectic is entirely erroneous. This is rather the appearance of patients who are suffering from an advanced consumption. In this connection we must remember

that consumption is more than tuberculosis. It is a mixed infection by the tubercle bacillus and the various pus bacteria, and it is the pyemia produced by the latter that rapidly undermines the health and strength of the patient. This patient is found to have but a slight elevation of temperature, 99.5° F. at 5 p.m., and from this fact we can safely infer that the tuberculous infection is neither extensive nor very active.

It is exceedingly important, for both prognosis and treatment, that we ascertain the extent of the tuberculous infection, and especially whether it has already invaded the intrapelvic genital organs. The finger in the rectum shows that the right side of the prostate is very hard and thickened; the left side is apparently normal. As the patient experiences no undue frequency or pain in urination, and as the urine is entirely free from pus, we may infer that the tuberculous infection has not as yet invaded the mucous surface of the prostate.

This is, then, a case of so-called primary genital tuberculosis, beginning, as usual, in the epididymis. We know, however, that the real primary tuberculous focus in these cases of so-called primary infection is almost invariably found in the lymph-glands connected with the respiratory or the intestinal tract, the mediastinal or mesenteric lymph-glands. Genital tuberculosis is primary only in the sense that it is the earliest accessible location of the infection, and this is a most important fact to remember in deciding upon the wisdom of surgical interference, as I shall explain presently.

This patient tells me that the trouble in the right side began about nine months ago, and on the left side about five months ago. Of course, that means that he first noticed it nine months ago; how long there may have been a tuberculous nodule in the epididymis before that time is a matter for speculation. Furthermore, I should like to call your attention to a very important matter,—the patient's age. Tuberculosis of the epididymis is favored, as is tuberculosis everywhere in the body, by arterial hyperemia. The disease will, therefore, be found most commonly in the epididymis during that time of life when the arterial blood-supply of the sexual organs is maintained at a very high grade. We know that prior to puberty the testicles and epididymes are undeveloped organs, which receive relatively little blood, just enough for their nourishment. During

the change which we call puberty, beginning at the fourteenth or fifteenth year of life, the testicle receives more blood than is necessary for its nourishment because it is beginning to carry on most important functions. It is, then, during the period of puberty that the blood-supply of the sexual organs is especially well developed, and it is during these years that we expect to find tuberculosis most frequently in the epididymis. As a matter of clinical experience it is during this time that tuberculosis most often develops in the epididymis, from the fifteenth to the thirtieth year. This man is 32 years of age, but, of course, no one can tell whether the infection on the right side dates back only nine months or one or two years; still it is in the immediate vicinity of the age limit. Again, it is by no means impossible for tuberculosis to occur at a later period in life, although the most frequent time is between the ages of 15 and 30 years.

When the infection finally makes its way along the ejaculatory duct into the urethra, there is apt to be an escape of more or less pus from the urethra. And you can see how easy it is for the physician, especially if he has never had his attention called to this matter, to make an error in diagnosis and call the case one of gonorrhea. Suppose a man, of about 22, comes to the physician and says that he has a purulent discharge from the urethra. What does the doctor think of first? Gonorrhea, and in the majority of cases he is right, but in the small minority of cases that purulent discharge will on careful examination be found to contain tubercle bacilli and no gonococci. The discharge is simply tubercular pus which, as is usual in such cases, is mixed with the ordinary pus bacteria. Such errors in diagnosis are by no means impossible, and have occurred a number of times to my own knowledge.

When the disease gets as far as the prostatic urethra the patient begins to exhibit symptoms of urinary distress, such as frequent and painful urination. In this case there would also be pus in the urine. That gives us a trio of symptoms which is quite significant and which should always direct the physician's attention to the possible existence of a tubercular lesion in some part of the sexual apparatus.

Our patient has a beginning tuberculosis on the left side and an advanced tuberculosis on the right side, but it has not yet reached the mucous surface, because his urine is entirely free from pus,

which would not be the case if the tubercular process had already extended to the mucous membrane of the urethra or its immediate vicinity. If it had, there would in all probability be pus and also blood in the urine. Here (holding up a bottle) is a specimen of urine from a case in which the infection has already reached the mucous surface. The patient is now urinating every hour or half hour, urination is very painful, and the urine contains a very large amount of pus and considerable blood.

CASE III.—The third patient is a man, 65 years of age. The left side of the scrotum is visibly enlarged. By palpation we discover that the enlarged tissues are the testicle and especially the epididymis in its lower segment. Hence it is reasonably certain, without consulting his history, that this is an infection of the epididymis primarily, and of the testicle secondarily, by a pus bacterium. On inquiry the patient tells us that he has for some months been obliged to urinate rather often, rising from two to four times at night for that purpose, and that his testicle swelled up about a week ago. The first of two glasses into which he passes his urine shows a distinct cloud of pus. Here we have, then, a pus infection of the prostatic urethra, which has recently invaded the right epididymis. As no instruments have been used in this case, this pus infection of the prostatic urethra is doubtless due either to enlargement of the prostate gland or to a rather tight stricture in the posterior segment of the urethra.

Although the patient's age would rather lead us to suspect an enlargement of the prostate gland, we find on a digital examination made by the rectum that there is no material enlargement of the rectal surface of the prostate, though this does not, of course, disprove the possibility that there may be an intravesical growth of the prostate. We find, however, a stricture at the bulb of the urethra (the most frequent location of urethral stricture) which will barely admit a No. 19 French sound. This is a sufficient explanation of the pus infection of the urethra behind the bulb (including the prostate), and hence of the secondary extension to the epididymis.

Pus infection of the epididymis, the so-called epididymitis, is a very common sequel to a tight stricture of the deep urethra, as well as to enlargement of the prostate, especially when the patient

habitually uses a catheter; it occurs without apparent cause, the cause being really the pus infection of the deep urethra.

CASE IV.—The fourth patient is a man, 37 years old, presenting an enlargement of the right side of the scrotum. On palpation we find a fluctuating tumor, within which is a smooth, much enlarged testicle. This is plainly a hydrocele, secondary (hydroceles are usually secondary) to a disease of the testicle. You will notice that the enlarged testicle is smooth, of natural shape, and painless on pressure, the usual features of a syphiloma of the testicle.

The patient gives, on inquiry, a very clear history of a constitutional syphilis contracted about ten years ago. He took medicine for about a year and was pronounced "cured" by his physician. He has had no recognized syphilitic manifestations in the past eight or nine years, and therefore considered himself cured. It is to be hoped that you will never tell a patient with syphilis that he is cured, meaning that the syphilitic taint has been eradicated from his system. Doubtless some patients are really cured, but most of them are not, and no one is in the position to tell in advance who are the fortunate ones. Make it a practice to give your syphilitic patients two injunctions: (1) to take medicine for syphilis two months out of every year throughout their entire life; and (2) to tell every physician whom they may have occasion to consult concerning any obscure or chronic ailment in any part of their bodies, that they have had constitutional syphilis. Doubtless most of the disastrous results of a late syphilis could be averted by a general adherence to these two injunctions.

CASE V.—The last patient that I have to show you is a child, about 2 years of age, presenting a scrotal enlargement on the right side. Palpation shows that the enlargement is continued into and through the inguinal canal; evidently the tumor is a hernia. Upon inquiry made from the mother we learn that this swelling began about six months after the birth of the child. It is, therefore, an acquired and not a congenital hernia. An acquired hernia in a child of this age is usually the result of habitually straining to evacuate either the rectum or the bladder. In many cases you will find that the cause for this straining is a tight and adherent prepuce, as you see is the case in this child.

The treatment of this hernia is circumcision, without which all treatment of this case, even a radical operation for the hernia, will

be of no avail. Some years ago there was brought to me a boy, 4 years old, who had had a radical operation for a double inguinal hernia, but both ruptures had recurred. On examination I found that the child had a pin-hole opening. After he had been circumcised and wore pads over the inguinal canals the condition was completely cured. The hernias never recurred.

TREATMENT.—The treatment of these various cases is indicated by the respective causes.

Gonorrheal epididymitis is treated by the usual hygiene, including regular defecation, rest in bed for a few days, and then the support of the swollen epididymis by a "bike" suspensory or its equivalent. The primary infection in the urethra requires injection of the entire urethra with a 5 per cent. solution of argyrol (silver vitelline) four to six times a day, the injection being retained eight to ten minutes each time. This injection is made with a one ounce, hard-rubber ear syringe (blunt tipped). The patient, after having emptied his bladder, injects one ounce (30 c.c.) of the argyrol solution, relaxing his cut-off muscle by endeavoring to urinate while the liquid is being injected. In the intervals between these injections plain hot water may be injected in the same way, a dozen times a day, and hot sitz-baths of ten minutes duration each may be taken as often as practicable.

Guaiacol should be applied to the skin over the inflamed epididymis. In order to prevent desquamation the guaiacol should be diluted with olive oil (1 part to 3 parts), and one teaspoonful (5 c.c.) of this solution should be rubbed into the skin four times a day. Guaiacol is absorbed by the skin very rapidly; it is an excellent anesthetic and distinctly limits the inflammatory process. Internal medication is limited to quarter-grain doses of calomel (0.015 gram) with 5 grains (0.3 gram) of sodium bicarbonate, four to six times daily, for three days. Hot fomentations should be continually applied while the patient is in bed.

Tuberculosis of the genital organs of the male always requires constitutional treatment and sometimes even surgical treatment. The constitutional treatment consists of a dry atmosphere, forced feeding, bodily rest, and guaiacol in ten to twenty minum (0.6 to 1.2 c.c.) doses four times daily. This patient unfortunately is not in the position to secure a change of climate, nor even an out-door occupation, nor bodily rest, but we will instruct him to eat heartily

and take guaiacol. Many of these patients recover symptomatically under this treatment, even in the moist atmosphere that prevails in Chicago. When they can go to a dry, sunny climate and live out-doors their prospects for health are excellent—so long as they remain in the dry climate.

Shall we excise the tuberculous foci? To this question diverse answers are given by different surgeons. Excision of the tubercular epididymis, even with its testicle, does not eliminate the tuberculous foci from the patient's body; for, as in this case, the infection has already reached the prostate and the seminal vesicles, and operations on these organs are now practically abandoned, that is, so far as tuberculosis is concerned. Moreover the original focus is doubtless in the inaccessible mesenteric or mediastinal glands, and besides, the inability to withstand this infection is inherent and persistent. Excision of the healthy testicles should seldom, if ever, be done—their internal secretion is too valuable to the patient. Excision of the tuberculous epididymis, on the other hand, is often advisable because of the remarkably good effect produced on the remaining foci of infection. We shall advise this patient to take the constitutional treatment which I have already outlined and to have the epididymes removed at the earliest possible opportunity.

The epididymitis from pus infection requires essentially the same treatment as gonorrheal epididymitis. In our case the primary cause of the trouble—the stricture at the bulb—must, of course, be removed by gradual dilation with sounds. Injection of the entire urethra with argyrol (5 per cent.) or the yellow muriate of hydrastia (1 grain to the ounce; 0.06 to 30 c.c.) will hasten the restoration of the deep urethra to its original healthy condition.

Syphiloma of the testicle requires merely the usual constitutional treatment for syphilis, often combined with an iron tonic. Mercury bichlorid, $\frac{1}{64}$ of a grain (0.001 gram), and potassium iodid, 20 grains (1.3 gram), in water after each meal; and two teaspoonfuls (10 c.c.) of Basham's mixture before each meal, will soon cause the testicle to resume its normal size. Inunctions of mercurial ointment into the scrotum may expedite matters considerably. The secondary hydrocele is usually absorbed under this treatment, although sometimes tapping is found necessary.

The acquired hernia in this child will be treated by circumcision, and retention of the returned bowel by a home-made pad.

THE MODERN TREATMENT OF VARICOSE VEINS

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THE term "varicose veins" is applied to alterations in the superficial or deep veins, which manifest themselves by dilatation and tortuosity of the vein, and by the formation of tumors composed of these altered veins, and called varicose tumors. Varicose veins usually appear in the lower limb, and it is to this form of the complaint that I refer in this article.

As regards the pathogenesis and cause of this disorder, varicose veins, whether hereditary or acquired, appear to depend on an alteration that affects more especially the two inner layers of the wall of the veins, and that ends in phlebosclerosis through disordered nutrition.

Setting aside the mechanical causes, which are able by themselves to bring on venous dilatation, and the alterations that follow bad nutrition of the vein, we must take into special account the general causes that appear to have an action: varicose veins are often found in gouty or rheumatic patients; pregnancy produces them mechanically, and also probably owing to a change in the condition of the blood in pregnant women; but here again a more general cause governs the pathologic condition, since all pregnant women do not have varicose veins, and the latter do not always disappear at the end of pregnancy. For my part I think that varicose veins often result from a congenital lack of resistance and nutrition of the wall of the vein, which will only be brought into evidence when local or general mechanical causes shall have thrown a strain on it at some moment in the patient's career.

From a clinical point of view there are several different forms of varicose veins of the leg:

(1) Tortuous dilatation of the large superficial veins of the leg, without varicose tumor. The skin is in good condition. In the way of functional symptoms, there are pain, or rather heaviness,

fatigue through long standing or walking, and in some cases edema of the ankles in the evening. Examination shows that although the veins are dilated there is no insufficiency; the valves still fulfil their functions and are not forced; when a flip of the finger is given to the internal saphena on the thigh, the wave does not extend along the vessel down to its origin in the leg. This clinical form, more or less marked, is very common, and may, owing to proper treatment, remain stationary for a long time.

(2) The condition just described is here complicated with varicose tumors, either of the leg or thigh; a favorite point is the inner side of the inner angle of the knee. These tumors may either be painless, or may become painful and inflamed, constituting attacks of varicose phlebitis.

(3) When there are varicose tumors there is almost always valvular insufficiency. Look for this insufficiency either by the flip of the finger method, or in the following way: raise the limb vertically, the patient lying in a horizontal position, and you will see that the varicose veins will rapidly empty themselves of the blood they contain and collapse, leaving a furrow where before there had been an elevation; keeping the leg still vertical, press on the inner saphena at the top of the thigh and get your patient either to sit up or stand up. Then let go your pressure, and you will immediately see the entire superficial venous system fill up again by reflux from the top downward. If the valves are in proper order repletion takes place slowly from below upward. The venous system of the lower limb, the lower vena cava, and the heart, form a system of communicating vessels that is just as much affected by the laws of gravity as anything else.

When varicose veins have reached the point of which we have just been speaking they are no longer as readily borne as the previous forms; the patient suffers, gets easily tired, is often troubled by edema, and is exposed to complications, trophic disorder of the skin, ulcers, neuritis, etc.

(4) Extensive dilatation is not necessarily synonymous with insufficiency, as there is a form of varicose veins in which the sclerosis and thickening of the walls give to the superficial vessels the consistency of pipe-stems to the touch; and just as we find in arterial atheroma, section shows that their caliber is much reduced, and yet the valves are sufficient. In this variety, which is often combined

with arteriosclerosis, cutaneous lesions, dermatitis, and ulceration are common, and the disorder becomes a complicated one.

(5) Without dilatation or tortuosity of the superficial veins, the patient may complain of a sensation of weight, and may easily grow tired from standing or walking; his feet may swell a little at night, and there may be capillary varicose veins to be seen on the surface of the leg, but of real varicose veins not a trace. When the muscular mass of the calf of the leg is shaken it may be slightly painful. In these cases there are almost always deep varicose veins without any superficial ones.

(6) In a last form, the patient complains a great deal, suffers from cramps, laminating pains, and is easily tired, the lower limbs swell up, and examination shows us that the legs, in which the adipose tissue is more or less well developed, have on their surface a quantity of small venous stars which give it a bluish tint. There may be here and there a few superficial dilatations. This is one of the worst forms; it is the cyanotic variety of the varicose condition.

Without going into the details of the complications of varicose veins, I may briefly say that these may consist in external or interstitial rupture, dermatitis, eruptions of different kinds, ulcers, neuritis, and phlebitis; ulcers and elephantiasis may lead the surgeon to counsel amputation to their unfortunate victim. Varicose veins should therefore be treated.

MEDICAL TREATMENT

A very large class of these patients require no more than hygienic or orthopedic treatment. It can be said that well-to-do people, who are not obliged to do heavy work, to stand up for long periods of time, or to fatigue themselves, can keep their varicose veins in hand, even if they cannot cure them, by the use of hygiene and bandages. It is in this way, in such patients, that all varicose veins with manifest insufficiency, with or without varicose tumor, should be treated when they do not give rise to attacks of phlebitis or to pain. In such cases we advise the patients to avoid long spells of standing up, as well as long walks, but always to walk rather than stand; to wash night and morning the affected leg, or the two legs, which are often equally affected, with a lead solution; to resort to local and general hydrotherapy, and to wear an elastic stocking that will come more or less high up according to the case, with

socks, or else each morning before getting up to apply in the proper way a suitable bandage, either of flannel cut diagonally, or of crêpe Velpeau. When the patient is clearly of a gouty constitution it will be advantageous to put him on a general course of treatment, and you can also administer, though without too much confidence, *hamamelis virginica* in the form of tincture or extract, 30 to 60 drops of tincture, or 10 to 15 centigrams (1.5 to 2 grains) of extract, a day. When patients are not subjected to fatigue, and can take the rest required, as well as suitable hygienic precautions, the situation improves, pain and heaviness disappear, and at the same time the edema lessens or even disappears; the varicose veins remain, but give very little trouble. In this connection it is interesting to note that it is always very marked cases of varicose dilatation that give the least functional trouble, and you will often be consulted by patients with enormous varicose veins who come to you for something entirely different, but not for this infirmity, which gives them no trouble at all.

The choice of an elastic stocking is important enough to merit our attention a moment. It should be made of a supple, elastic tissue, equally resistant at all points, and should begin at the root of the toes and almost always come up above the knee. It should not press too strongly, nor in an unequal manner, as in that case it will almost always do more harm than good; it should be put on in the morning and taken off at bedtime. When the varicose veins extend to the thigh, above the knee, it is customary to add a thigh-piece to the stocking, either as a single article or separately. The thigh-piece is almost always useless, and often harmful, as it is difficult to adjust, on account of the conical shape of the thigh, rolls up on itself in spite of every device to prevent this, and then brings unequal pressure to bear—for which reasons it is best not to use it. In addition to the ordinary elastic stocking a laced elastic stocking is often used, which will enable you to follow the variations in volume of the limb, and to bring greater or less pressure to bear, according to indications.

Stockings of dog-skin, which is supple and slightly elastic, are sometimes more suitable than elastic stockings, which some persons cannot tolerate.

Unfortunately hygiene and orthopedics are often not sufficient in persons whose social condition obliges them to do heavy work,

to stand, to walk, and to undergo fatigue whether they will or not. Bandages soon lose their strength, and are then of no further use, even when they do not do harm by bringing unequal pressure to bear, or by damaging the skin. It is in such cases that surgical intervention is indicated.

SURGICAL TREATMENT

Surgical operations can be divided into three groups when the varicose veins are not complicated; we will only consider this eventuality.

(1) Ligatures at different heights, with resection of one or both saphenous veins.

(2) Ligatures with venous resection, combined with the removal of varicose tumors of varying sizes.

(3) Ligatures at different heights, with resections, combined with the removal of large flaps of skin containing in their thickness a varying quantity of varicose veins.

These operations are suited to different clinical forms.

(1) The principal indications of the ligature at different heights with resection of pieces of the vein are the presence of serpentine varicose veins without tumors, or flaccid dilatation of the vessels and valvular insufficiency. This is always a high-tension form, and often gives rise, as we have already said, to pain, edema, and fatigue.

The successive ligatures are generally 3, 4, or 5 in number, of which two are very important, one below the point where the saphenous joins the femoral vein, the other above the inner condyle of the femur. The rest can be placed on the thigh and leg, and the operation should be done with local anesthesia with a 1 per cent. solution of cocain. These successive ligatures also give good results, though less satisfactory, in cases of advanced sclerosis with thickening of the venous walls; there is then often an ulcer, or a tendency to ulceration, which is itself favorably influenced.

(2) The successive ligatures are combined with the removal of tumors when the latter exist with serpentine dilatations. In almost all such cases the resection of varicose tumors is long and difficult, and it is best to anesthetize the patient with ether or chloroform, especially if the resection is to be multiple or extensive, and if both legs are affected.

(3) For the last two years I have performed an operation which consists in combining successive ligatures with excision from the skin of the leg, less frequently of the thigh, of large flaps together with the subjacent varicose veins. The indication arises when the skin of the leg is flabby, extensible, without tone, resembling the skin of the scrotum in certain forms of varicocele. Reunion by first intention can be obtained. In this way is made a species of natural, elastic stocking, which appears to me to render still more favorable the results of the ligature at different heights; when the patient is cured he can get along perfectly well without an elastic stocking.

The results of the ligatures, and venous and cutaneous resections, are really excellent, and we can affirm that in many cases, especially with men who have to do heavy work, long marches, or who have to stand in the vertical position for long periods, a radical cure is effected, in the sense that although there may be some varicose veins left, all the functional troubles disappear entirely, and very often for good. In a word, these are very good operations.

FORMS OF VARICOSE VEINS THAT MUST NOT BE OPERATED ON

Varicose veins that develop during pregnancy should be treated by hygiene and orthopedics. Watch carefully the slightest lesion of the skin, which may be a possible opening for infection followed by phlebitis. These varicose veins often disappear spontaneously after confinement.

Patients with varicose dilatations, with cyanosis of the limb, and small capillary varicose veins, should not be operated on, as the result is almost always a failure.

It is very evident that any contraindication due to a general condition will be all the more one for the radical cure of varicose veins, which should only be undertaken in persons who are otherwise healthy. The coexistence of a varicose condition of the scrotum and spermatic cord, or of the veins of the rectum or of the anus, is not a counterindication for a radical cure of varicose veins; but their presence should make one circumspect in the decision to be taken.

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THE THIRST AND NAUSEA OF ANÆSTHESIA

are entirely prevented, and the shock of surgical operation greatly relieved by high rectal injections of

Bovinine

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Professor of Anatomy and Chirurgery, University of Dublin.

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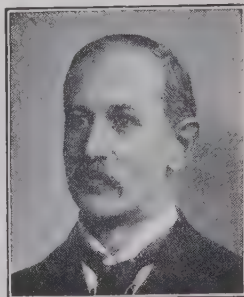
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Opie

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Associate in Pathology in the Johns Hopkins University; Fellow of the Rockefeller Institute of Medical Research.

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SCANT space is devoted to Diseases of the Pancreas in text-books of Medicine and Pathology, hence the necessity for this work on the cause and nature of Disease of the Pancreas, which gives the Anatomy, Anomalies, and Histology of the Pancreas, the Symptoms and Treatment of Pancreatic Diseases, a large Bibliography, and complete index.

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Conditions peculiar to the organs have received most attention, and throughout the work are numerous references to the symptomatology of pancreatic disease. Since lesions of the pancreas are seldom primary, their clinical manifestations are obscured by accompanying diseases of adjacent organs, and the recognition of pancreatic lesions, their cause and their consequence is of great importance, not only to the physician, but notably to the surgeon who opens the abdomen, while to the student of internal medicine few conditions present greater difficulties than do the various forms of pancreatic disease; but, with the increasing knowledge of their pathology, their nature, and their relation to other diseases, means for their recognition are closer to hand.

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7. The Varieties of Chronic Interstitial Pancreatitis.

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Cooke A Nurse's

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Vaughan

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